

persisted for 1 year or more despite preservation of the continuity of the facial nerve during ablative procedures.

To treat patients with long-standing facial paralysis, we have applied neurovascular muscle transfer to obtain facial reanimation. The intervention differs from those for established facial paralysis resulting from conditions such as congenital dysfunction, Bell palsy, Hunt syndrome, or intracranial seventh nerve damage. This is because ablative surgery of the parotid region frequently results in a soft-tissue defect, which should be restored using a soft-tissue flap combined with the neurovascular free-muscle transfer. Moreover, selection of recipient nerves and vessels can be complicated by previous ablative surgery or intraarterial chemotherapy. The present study describes the operative procedure for neurovascular free-muscle transfer after ablative surgery in the parotid region and demonstrates some representative cases. In our series, either the gracilis or latissimus dorsi muscle was transferred in all cases. Differences between the two operative procedures and the results are also discussed.

PATIENTS AND METHODS

Patient Profiles

Between November of 1981 and February of 2001, neurovascular free-muscle transfer was performed in 45 patients with facial paralysis following ablative surgery in the parotid region. Patients ranged in age from 5 to 65 years (mean, 34.2 years) at the time of neurovascular free-muscle transfer. Facial paralysis was incomplete in 14 of the 45 patients. Ancillary procedures accompanying neurovascular free-muscle transfer included temporal muscle transfer for eyelid closure in 20 patients, lid loading using a gold plate for the upper eyelid in five, eyebrow lift in 17, and blepharoplasty in six.

Operative Technique

In almost all cases, a preauricular incision was used for primary ablative surgery. This incision was then reused to create a subcutaneous cheek pocket to accept subsequent neurovascular muscle transfer. Recipient vessels were then prepared. The superficial temporal or facial vessels were predominantly used. However, when these vessels were unsuitable for vascular anastomosis because of previous ablative operation, chemotherapy, irradiation, or other

such reasons, other vessels in the ipsilateral upper neck were used. If vessels in the ipsilateral neck were unavailable, contralateral vessels were selected as recipients. Vascular grafting was sometimes required in such cases.

Selection of the recipient nerve depends on the condition of the residual ipsilateral facial nerve. When the ipsilateral facial nerve stump was available, it was used as a motor source for innervating transferred muscle.¹¹ When the ipsilateral facial nerve was unavailable because of the location of the nerve stump deep in the facial nerve canal, contralateral facial nerve branches were used as recipients. In the early cases of our present series, a two-stage method combining neurovascular free-muscle transfer with cross-face nerve grafting¹² was performed. In the first stage of this method, a sural nerve graft between the intact side and paralyzed cheek was used. Approximately 1 year later, the selected muscle (predominantly gracilis, but also latissimus dorsi in some cases) was transferred in the second operation. The motor nerve of the transferred muscle was sutured to the stump of the cross-face nerve graft. After approximately 1995, a one-stage method using latissimus dorsi muscle has been used more commonly.¹³ The thoracodorsal nerve of latissimus dorsi was crossed through the upper lip and sutured to a contralateral facial nerve branch in one operation.

When soft-tissue defects required reconstruction because of extensive tumor resection, a soft-tissue flap was simultaneously performed with neurovascular free-muscle transfer. Musculocutaneous flaps using gracilis, latissimus dorsi, or serratus anterior were used for restoration of facial contour in our present series.

Transferred Muscle

Gracilis was used in 24 of the 45 patients, and latissimus dorsi was used in 21.

Selected Recipient Vessels

When gracilis was transferred, recipient vessels comprised superficial temporal vessels in 12 patients and facial vessels in 12. When latissimus dorsi was transferred, recipient vessels comprised facial vessels in 16 patients, the superior thyroid artery and superior thyroid or internal jugular vein in four, and contralateral facial vessels with interpositional graft of the radial vessels in one. In this last patient, ipsilateral vessels were unavailable because of previous ablative operation, radical neck resection,

and rectus abdominis musculocutaneous flap transfer for coverage of a skin defect following cancer ablation.

Selected Recipient Nerves

When gracilis was used, cross-face nerve grafting was performed before muscle transfer in 22 patients, whereas the ipsilateral facial nerve stump was used as the recipient nerve in the remaining two. When latissimus dorsi was used, recipient nerves comprised the ipsilateral facial nerve stump in three patients and the cross-face nerve graft stump that had been grafted before muscle transfer in six. In 12 patients, the thoracodorsal nerve of the latissimus dorsi muscle, approximately 15 to 16 cm long, was crossed through the upper lip and sutured to contralateral facial nerve branches exposed anterior to the parotid gland.

Soft-Tissue Augmentation

When gracilis was used, a dermal fat flap overlying the muscle was used for cheek augmentation in one patient. Gracilis was used solely for facial reanimation in the other 23 patients, without soft-tissue augmentation in the parotid region. When latissimus dorsi was used, a dermal fat flap overlying the muscle was transferred simultaneously with the muscle segment in one patient. A deepithelialized serratus anterior musculocutaneous flap nourished by a common trunk with the thoracodorsal nutrient vessels of the latissimus dorsi was transferred in two patients for cheek augmentation.

Evaluation

The aims of this operative procedure were reconstruction of a natural or near-natural smile and augmentation of the depressed

cheek with soft tissue. The grading scales shown in Table I were used to evaluate smile reconstruction.

RESULTS

In two patients with gracilis transfer and three patients with latissimus dorsi transfer, voluntary contraction of grafted muscle was not observed. In one patient with gracilis transfer and one patient with latissimus dorsi transfer, acquired muscle contraction was excessive, resulting in unnatural animation of the smile. In both cases, recipient nerves were ipsilateral facial nerve stumps that had been dissected by opening the facial nerve canal in the mastoid process.

Smile results for patients with gracilis transfer were evaluated as grade 5 in 10 patients (42 percent), grade 4 in 10 patients (42 percent), grade 3 in two patients (8 percent), and grade 1 in two patients (8 percent). Results for latissimus dorsi transfer were evaluated as grade 5 in nine patients (43 percent), grade 4 in eight patients (38 percent), grade 3 in one patient (5 percent), and grade 1 in three patients (14 percent).

CASE REPORTS

Case 1

A 43-year-old man presented with complete left facial paralysis resulting from ablative surgery of facial nerve schwannoma in the parotid gland 1 year previously (Fig. 1). The one-stage method using latissimus dorsi muscle was planned for smile reanimation. A preauricular incision from the previous operation was reused to create a subcutaneous cheek pocket to accept subsequent latissimus dorsi transfer. Because detailed information from the previous ablative surgery was unavailable, the ipsilateral facial nerve was not used and the contralateral facial nerve branches were selected as recipient nerves. The facial vessels were used as recipient vessels. After transfer of the latissimus dorsi, endoscopic eyebrow lift was performed for eyebrow ptosis, and the upper eyelid was

TABLE I
Evaluation Criteria

Grade	Description
5	Symmetric balance and good facial tone at rest; sufficient muscle power on voluntary contraction; synchronous and natural expression on emotional facial movements, especially on smiling; EMG demonstrating relatively high amplitudes, with full interference patterns and high evoked potential obtained on stimulation of the contralateral facial nerve
4	Symmetric balance and good facial tone at rest; active muscle contraction acquired but not sufficiently synchronous (too strong or slightly weak); EMG demonstrating good interference patterns and evoked potentials; results well accepted by the patient
3	Symmetric balance and good facial tone at rest; insufficient contraction of the muscle; low volitional EMG spikes with discrete interference patterns
2	Reduced symmetric balance on smiling; no effective contraction of the muscle; EMG with no interference patterns
1	No correction; electrically silent EMG
0	No follow-up

EMG, electromyography.



FIG. 1. A 43-year-old man with complete left facial paralysis caused by ablative surgery of facial nerve schwannoma. Preoperative appearance at rest (*above, left*) and smiling (*above, center*). (*Above, right*) The latissimus dorsi muscle was transferred into a cheek pocket. The contralateral facial nerve branches were selected as recipient nerves and the facial vessels were used as recipient vessels. (*Below*) Five-year postoperative appearance at rest and smiling after surgical revision that was performed 2 years after the neurovascular free-muscle transfer.

loaded with a gold plate for eye closure. Muscle contraction was first recognized 6 months after neurovascular free-muscle transfer. Surgical revision to change the position of muscle attachment was performed 2 years after neurovascular free-muscle transfer. As of 5 years after neurovascular free-muscle transfer, smile result was grade 5.

Case 2

A 49-year-old man presented with complete right facial paralysis resulting from radical parotidectomy and partial mandibulectomy for recurrent mucoepidermoid carcinoma of the parotid gland (Fig. 2). No radiotherapy or chemotherapy had been performed before facial nerve reconstruction. Because the ipsilateral facial nerve was located in the facial nerve canal of the temporal bone, contralateral facial nerve branches were used as recipient nerves. In the first operation, a cross-face nerve graft using a sural nerve segment

was grafted through the chin, with concomitant transfer of temporal muscle to the eyelids for eye closure and juxta-brow excision for brow lift. Ten months later, when Tinel's sign had advanced to the end of the grafted nerve, neurovascular free-muscle transfer was performed. Because a depressed deformity of the parotid region was evident following the ablative surgery, a deepithelialized serratus anterior musculocutaneous flap was transferred for soft-tissue augmentation in combination with a latissimus dorsi musculocutaneous flap for facial reanimation. The thoracodorsal vessels nourishing both flaps were anastomosed to the facial vessels and the thoracodorsal nerve was sutured to the cross-face nerve stump. As of 2 years 4 months after neurovascular free-muscle transfer, the patient was satisfied with the results after secondary corrective surgery in which transferred muscle was shortened at the nasolabial fold line. Because the transferred muscle is still weak, the smile result was grade 4.

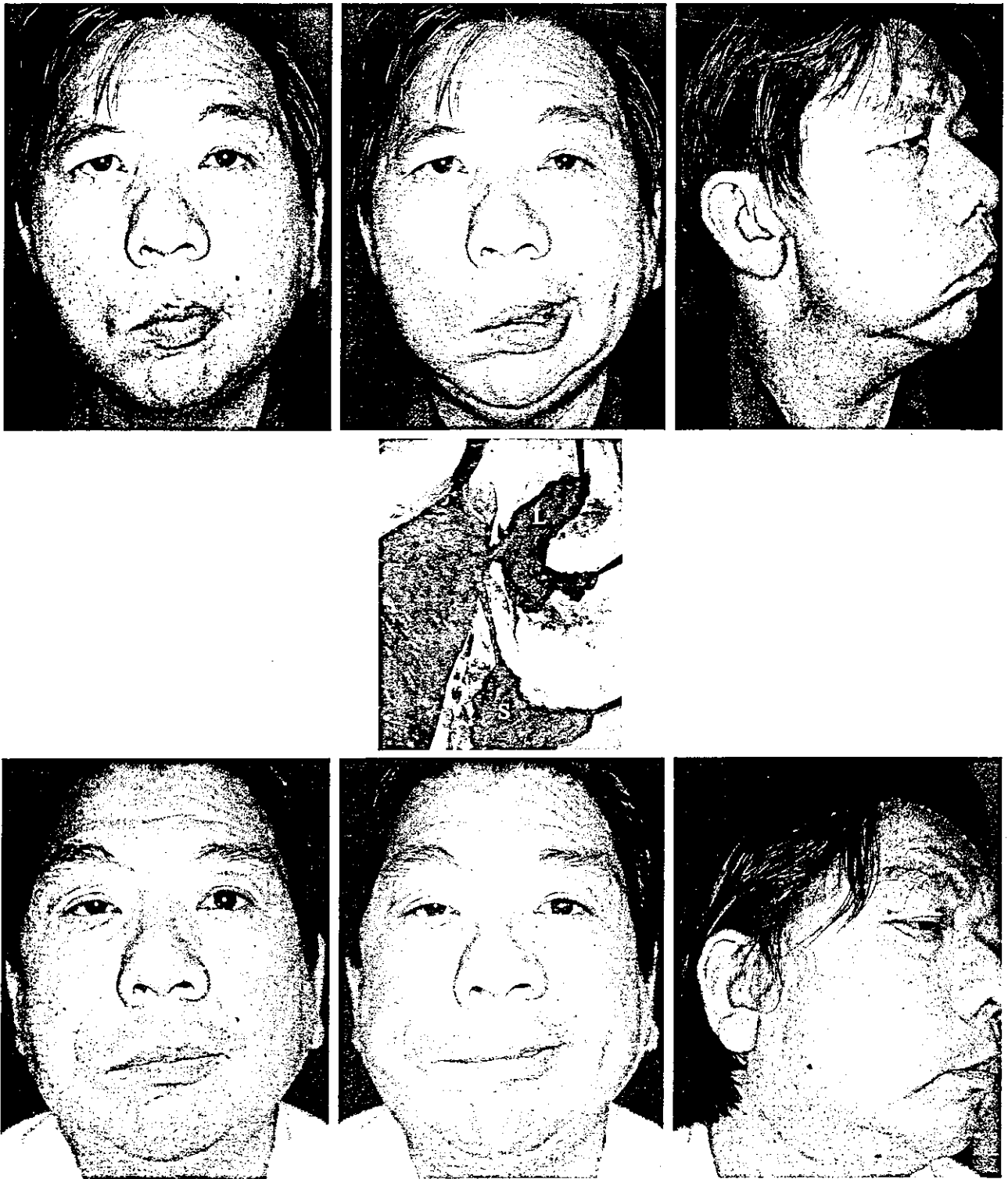


FIG. 2. A 49-year-old man with complete right facial paralysis caused by radical parotidectomy and partial mandibulectomy for recurrent mucoepidermoid carcinoma of the parotid gland. (Above) Preoperative appearance at rest and smiling. A depressed deformity of the parotid region was evident. (Center) A deepithelialized serratus anterior musculocutaneous flap (S) was transferred for soft-tissue augmentation in combination with a latissimus dorsi muscle (L) for facial reanimation. (Below) Two years 4 months postoperatively; appearance at rest and smiling after secondary corrective surgery.



FIG. 3. A 54-year-old woman with complete right facial paralysis resulting from ablative surgery of squamous cell carcinoma of the right external ear canal. Preoperative appearance at rest and smiling. A severe deformity of the lower face and neck was evident.

Case 3

A 54-year-old woman underwent ablative surgery for squamous cell carcinoma of the right external ear canal (Fig. 3). Resection of the external ear, parotid gland, zygomatic arch, mastoid process, and mandible was performed, along with radical neck dissection. Skin and soft-tissue defects were reconstructed using a rectus abdominis musculocutaneous flap, resulting in complete facial nerve palsy with severe deformity of the lower face and neck. Intraarterial chemotherapy and radiotherapy were performed preoperatively and postoperatively, respectively. One year after ablative surgery, she was referred to us for facial reconstruction. The one-stage method using the latissimus dorsi was planned for facial reanimation. Because vessels suitable for vascular anastomosis were unavailable in the ipsilateral face and neck, contralateral facial vessels were used with an interpositional graft of the radial vessels taken from the left forearm (Fig. 4). Contralateral facial nerve branches were used as recipient nerves. Peripheral Z-plasties to the operative scar of the previous neck dissection and muscle reduction with defatting of the rectus abdominis musculocutaneous flap that had been transferred previously in the ablative surgery were performed simultaneously. Right medial canthal plasty and upper eyelid loading with a gold plate were also performed. As of 1 year 7 months postoperatively, movement of transferred muscle was obtained and the smile result was grade 4 (Fig. 5).

Case 4

A 52-year-old woman presented with complete right facial paralysis following ablative surgery for recurrent pleomorphic adenoma (Fig. 6). Because the ablative surgery had been performed 2 years earlier, neurovascular free-muscle transfer was performed using gracilis for smile reconstruction. The ipsilateral facial nerve stump was initially sought in the scar tissue but could not be found. The mastoid process was then burred to open the facial nerve canal, exposing the proximal stump of the facial nerve for nerve suture. The motor nerve to the gracilis was sutured directly to the facial nerve trunk. Facial vessels were selected as recipients and were anasto-

mosed with the nutrient vessels of the gracilis. The patient presented at our hospital 7 months postoperatively, and excessive contraction of the transferred muscle and bulkiness of cheek skin was evident (grade 4), requiring surgical revision. Transferred muscle was debulked after cheek skin had been undermined to eliminate abnormal facial creases. Furthermore, the nasolabial fold was incised to release the muscular attachment, which was then repositioned using the fascia lata 1 year later. As of 3 years postoperatively, the smile result improved to grade 5.



FIG. 4. Because vessels suitable for vascular anastomosis were unavailable in the ipsilateral face and neck, radial vessels (R) were interposed between the contralateral facial vessels that were selected as recipients and the thoracodorsal vessels (T).



FIG. 5. Postoperative appearance at 1 year 7 months, at rest and smiling. Contour of the lower face and neck was well restored.

DISCUSSION

Since Harii et al.¹⁴ first reported the use of neuromuscular free gracilis muscle transfer for the treatment of long-standing facial paralysis, numerous reconstructive surgeons have used neurovascular free-muscle transfer as the preferred method for treating long-standing facial paralysis.^{13,15-18} In our present series, neurovascular free-muscle transfer was successfully used to treat established facial paralysis following ablative surgery in the parotid region. However, several difficulties exist in this kind of facial reconstruction that are not encountered with reconstruction of established facial paralysis resulting from conditions such as congenital dysfunction, unresolved Bell palsy, Hunt syndrome, or intracranial damage.

Fewer vessels are suitable for microvascular anastomoses, because of radical resection during ablative surgery and/or intraarterial chemotherapy. The superficial temporal or facial vessels that are typically selected as recipient vessels are frequently unavailable. Nutrient vessels for the gracilis muscle are not particularly long and cannot reach suitable vessels in the neck. Gracilis should therefore not be used as a donor muscle when superficial temporal or facial vessels are unavailable. Conversely, nutrient vessels for the latissimus dorsi are long enough to reach vessels in the upper neck area such as the superior thyroid vessels. In reconstructions following radical ablation for parotid tumors, particularly those including neck dissection, use of the latissimus dorsi is prefer-

able to gracilis from the perspective of potential recipient vessels.

Attention must be paid to selecting the recipient nerve. In our series, when the ipsilateral facial nerve branch was available, it was used as a motor source for innervating transferred muscle. Of five patients in whom ipsilateral facial nerves were used, two demonstrated excessive muscle contraction resulting in an unnatural appearance during muscle function. The recipient ipsilateral facial nerve stump for both of these patients was exposed by opening the facial nerve canal in the mastoid process, and the facial nerve main trunk was directly sutured to the motor nerve of the transferred muscle. In the remaining three patients in whom a near-natural smile was achieved without unnatural muscle contraction, the muscle motor nerve was sutured to the stumps of facial nerve branches in the cheek. In a previous report, we reported that unnatural muscle contraction was not seen in 39 patients who underwent muscle graft using the facial nerve on the affected side as a motor source.¹¹ However, the two patients described here were encountered after that report. Chuang et al.¹⁹ presented four cases in which transferred muscle reinnervated using the ipsilateral facial nerve displayed excessive contraction over time. Because local anesthesia can temporarily relieve muscle tightness, they suggested that excessive reinnervation of the muscle appeared largely responsible for such contracture. However, Harrison noted that fibrous tissue created by



FIG. 6. A 52-year-old woman with complete right facial paralysis following parotidectomy for a recurrent pleomorphic adenoma. Preoperative appearance at rest (*above, left*) and smiling (*above, center*). (*Above, right*) The harvested latissimus dorsi muscle was divided into two segments, one of which was inserted into a cheek pocket as a neurovascularized muscle for facial reanimation, and the other of which was used with denervation of the thoracodorsal nerve branch for soft-tissue augmentation in the parotid region. (*Below, left*) Postoperative appearance at 7 months while smiling. Excessive contraction of the transferred muscle and bulkiness of cheek skin was evident. Postoperative appearance at 3 years, at rest (*below, center*) and smiling (*below, right*) after revisional operations including debulking.

surgical dissection and the natural biodegradation that occurs before reinnervation may contract with the muscle.²⁰ Our results seem to support the excessive reinnervation theory of Chuang et al., as two patients in whom the facial nerve trunk was used as the recipient nerve displayed excessive muscle contraction, whereas three patients in whom facial nerve branches were used as recipient nerves demonstrated natural contraction. The facial nerve trunk might be responsible for excessive innervation of the muscle. In three of four patients (excluding a case of Romberg hemifacial atro-

phy, in which neurovascular muscle transfer may not have been indicated) reported by Chuang et al., the facial nerve trunk was used as the recipient nerve. We therefore presently believe that when a branch of the ipsilateral facial nerve is available in the cheek, it should be used as a recipient nerve, but we do not recommend use of the facial nerve trunk. The contralateral facial nerve branch should be used when the facial nerve trunk is the only ipsilateral option available.

When depression deformity caused by previous tumor ablation in the parotid region is

conspicuous, soft-tissue augmentation is required. As noted before, gracilis muscles were transferred in the early cases of our present series, when latissimus dorsi muscle transfer was not yet developed. However, dermal fat flaps over the gracilis muscle cannot be adequately set into the defect, as the fat flap over gracilis is difficult to elevate separately from the muscle segment as a composite flap. This is the reason why a dermal fat flap in combination with the gracilis muscle was transferred in only one case for soft-tissue augmentation. On the contrary, many authors have reported that the latissimus dorsi flap can be elevated as a combined flap with other flaps such as the serratus anterior flap and the scapular flap on a single pedicle.²¹⁻²⁴ Kimata et al.²⁵ reported a case of facial reconstruction using a combination of parascapular flap and latissimus dorsi muscle flap for facial reanimation and soft-tissue augmentation in the parotid region. In our series, a deepithelialized serratus anterior musculocutaneous flap was used for two patients. The thoracodorsal vessels divide into branches to nourish both the latissimus dorsi and serratus anterior muscles. The latissimus dorsi and serratus anterior musculocutaneous flap for soft-tissue augmentation can therefore be harvested as a combined flap for facial reanimation and soft-tissue augmentation, respectively.²⁶ The serratus anterior musculocutaneous flap may therefore represent the best option for combination with latissimus dorsi transfer, as intraoperative repositioning of the patient is not required, unlike when the scapular flap is used.

CONCLUSIONS

The results of this present series show that the latissimus dorsi muscle represents a better choice than the gracilis muscle for the reconstruction of facial paralysis after ablative parotid surgery, from the perspective of recipient vessels and combined soft-tissue flap, even though no significant difference in acquired smile function of the paralyzed face was evident between the two methods. When the contralateral facial nerve is selected as the recipient nerve, gracilis muscle should typically be used in a two-stage procedure with a cross-face nerve graft, although some authors have reported the use of the gracilis muscle in a one-stage method.^{27,28} Conversely, the latissimus dorsi muscle is used in a one-stage procedure, as sufficient thoracodorsal nerve can be har-

vested to reach the contralateral cheek without nerve grafting. As a result, the latissimus dorsi muscle offers the benefit of a shorter recovery period than the two-stage method using the gracilis muscle.¹³ Use of the latissimus dorsi muscle is therefore recommended over the gracilis muscle when the ipsilateral facial nerve branch is unavailable.

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Prevention of Denervation Atrophy by Nerve Implantation

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ABSTRACT

Prevention of denervation atrophy in skeletal muscle by nerve implantation to a muscle belly was studied in a rat model. In the animals' legs, the tibial nerve branch innervating the lateral head of the gastrocnemius muscle was transected, and subsequently repaired by either simple nerve suture ($n=20$) or interpositional nerve grafting ($n=20$). The tibial nerve branch innervating the medial head was dissected out. The peroneal nerve was transected and implanted directly to the lateral head of the gastrocnemius muscle on one side and, as a control, the nerve on the other side was cut. After 6 months, isometric tension of the gastrocnemius muscle was greater on the implantation side than on the control side in the nerve-suture group ($p < 0.05$), but no tension difference between the two sides was observed in the nerve-graft group. The effects of neurotization by an implanted nerve may compete with those by a repaired nerve, when neurotization of the latter is delayed. Only when the time interval between neurotization by an implanted nerve and reinnervation by a repaired original nerve is short, does nerve implantation attenuate denervation atrophy.

KEYWORDS: Denervation atrophy, nerve implantation, direct neurotization

Periods of muscle denervation are known to influence reinnervation; that is, the longer the period of denervation, the less reinnervation progresses.¹ Conversely, if the period of denervation is shortened, reinnervation is expected to progress well. Attempts have been made to prevent denervation atrophy. Electrostimulation of paralyzed muscle can improve functional recovery,²⁻⁴ but the technical complexity of such stimulation has prevented its common use. Another method, the babysitter procedure, was introduced by Terzis.⁵ Using this method, the hypoglossal nerve is sutured to the facial nerve, which serves as a temporary motor source to prevent denervation atrophy in facial paralysis. This procedure is quite appealing; however, a drawback is that the nerve suture must be repeated to replace the motor nerve supply.

We believe that use of direct nerve implantation as an alternative babysitter method may avoid this problem. Direct implantation of the nerve involves insertion of a motor nerve stump in a muscle belly. This makes reinnervation of the muscle possible (termed direct neurotization), but less active contractility is attained than with a nerve suture. Currently, direct neurotization is not a first choice in clinical practice. It does, however, result in relatively early muscle reinnervation.⁶⁻⁸ Therefore, we use it as an alternative method for preventing denervation atrophy.

The purpose of this study was to determine whether direct neurotization can provide a temporary motor source until neural neurotization by the original nerve occurs. Our model is different from Terzis' method in that direct neurotization, not

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neural neurotization, is used as the temporary motor source.

MATERIALS AND METHODS

Male Wistar rats weighing 250 to 300 g were used. Animals were housed, fed, and treated in accordance with the National Institutes' of Health *Guide for the Care and Use of Laboratory Animals*. After anesthetization with 40 mg/kg Nembutal (intraperitoneal injection), a short longitudinal incision was made on the posterior aspect of each animal's leg, exposing the gastrocnemius muscle and revealing the tibial nerve branches innervating the lateral and medial heads (Fig. 1A). The medial branch to the medial head of the gastrocnemius muscle was cut away to prevent possible innervation of the lateral head through this branch. The lateral branch to the lateral head was then transected and subsequently repaired by either direct nerve suturing (nerve-suture group) or by interpositional nerve grafting (nerve-graft group). Each group included 20 rats.

In the nerve-suture group (See Fig. 1B), the transected lateral branch was sutured directly by the epineurial suture method. In the nerve-graft group (See Fig. 1C), a 1-cm sural nerve graft was placed in a nerve gap created at the transected site of the lateral branch and was fixed in place by the epineurial suture method. The nerve-graft group was designed to delay reinnervation via the original nerve. Nerve repair was carried out with 10-0 nylon under the operating microscope. Next, the peroneal nerve was dissected and cut. On the left side (left leg, direct neurotization side), the proximal end of the dissected peroneal nerve was implanted into the lateral head by fixing the epineurium to the fascia with 10-0 nylon. On the right side (right leg, control side), the peroneal nerve was cut off.

Six months after surgery, the gastrocnemius muscle was evaluated in terms of physiology and histology. This period is long enough for both the implanted nerve and the sutured nerve to stabilize. Isometric tension of the gastrocnemius muscle was measured with an electrical strain gauge. After setting the pre-tension at

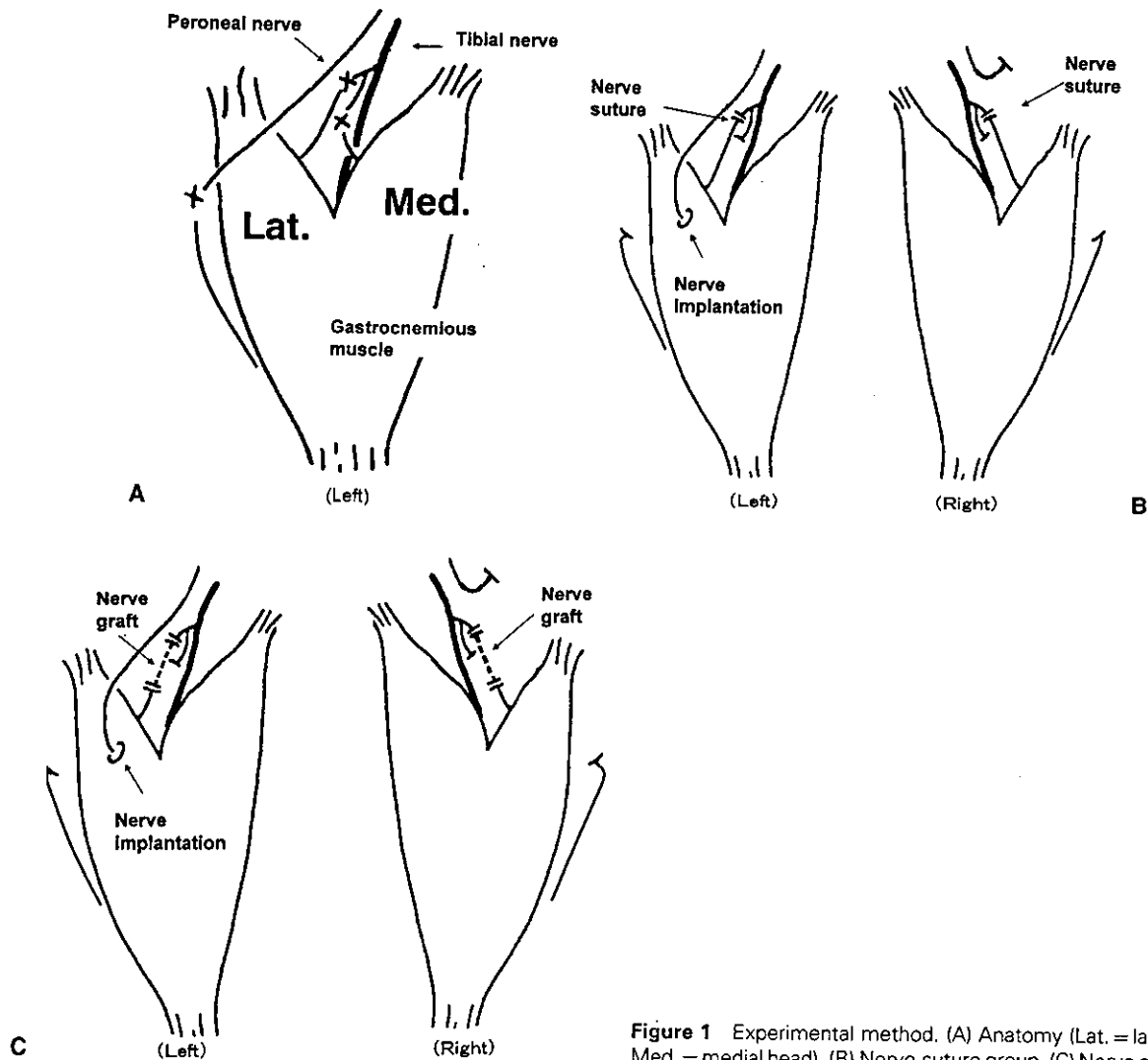


Figure 1 Experimental method. (A) Anatomy (Lat. = lateral head; Med. = medial head). (B) Nerve-suture group. (C) Nerve-graft group.

200 gm, isometric tension was measured by stimulating the sutured original nerve (tibial nerve) or the implanted foreign nerve (peroneal nerve). Tetanic stimulation of 30 Hz was used. Following physiologic evaluation, the

gastrocnemius muscle was harvested after sacrificing the rats by injection of a high dose of Nembutal. A specimen taken from the midpoint between the site of tibial nerve attachment and the site of peroneal nerve implantation

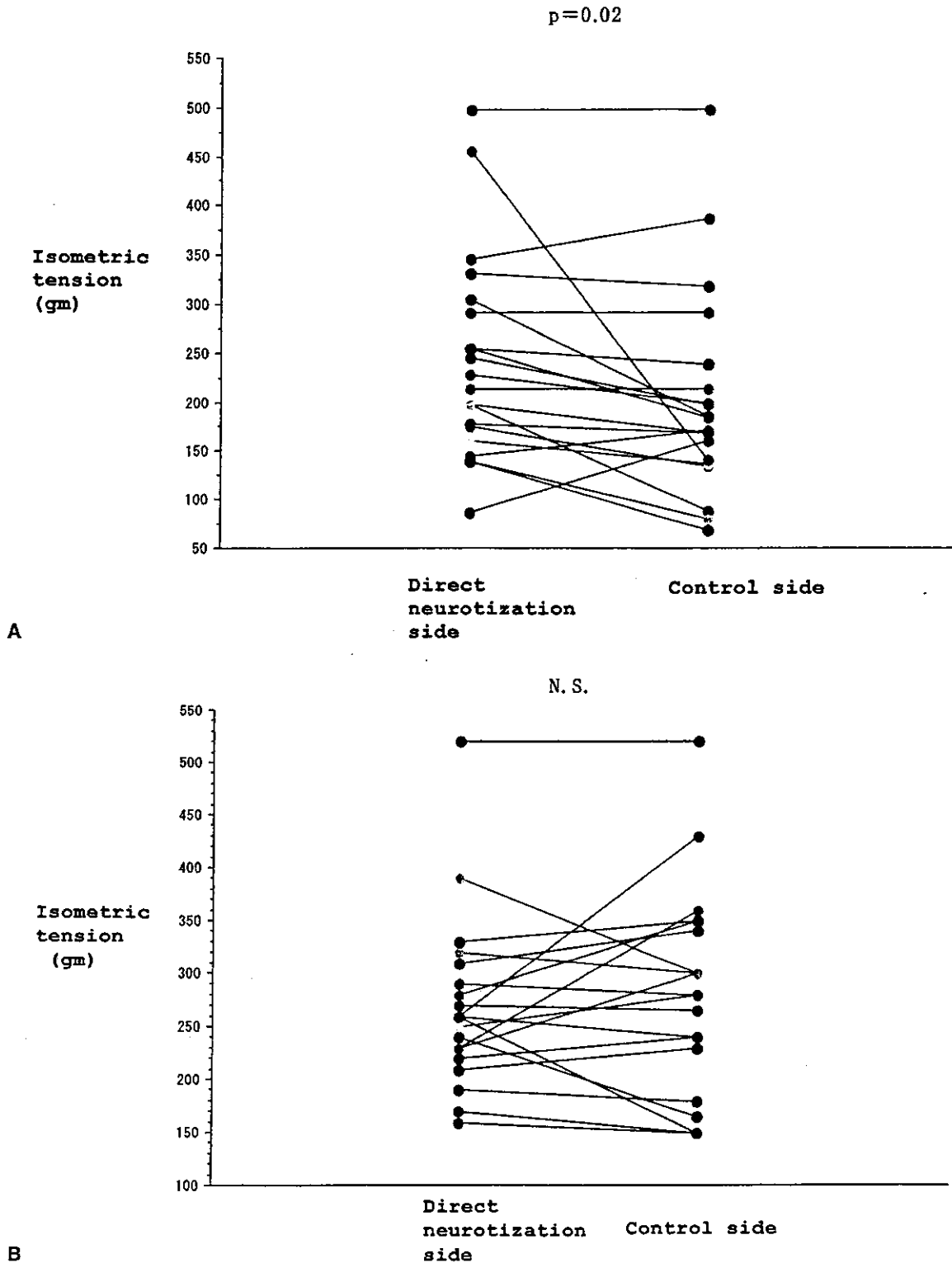


Figure 2 Plot of gastrocnemius muscle isometric tension for direct neurotization side and control side. (A) Nerve suture group. (B) Nerve graft group (N.S. = not significant).

was stained for actomyosin ATPase. With the use of an image analyzer, the length of the short axis was measured to determine fiber diameter in 300 muscle fibers.

The Wilcoxon test and Wilcoxon signed-rank test were used to determine statistical significance. A p value < 0.05 was considered to be significant.

RESULTS

Isometric tension induced by stimulation of the repaired original nerve was slightly greater (13 percent on average) on the direct neurotization side than on the control side in the nerve-suture group ($p = 0.02$, Fig. 2A), but no difference was seen between the two sides in the

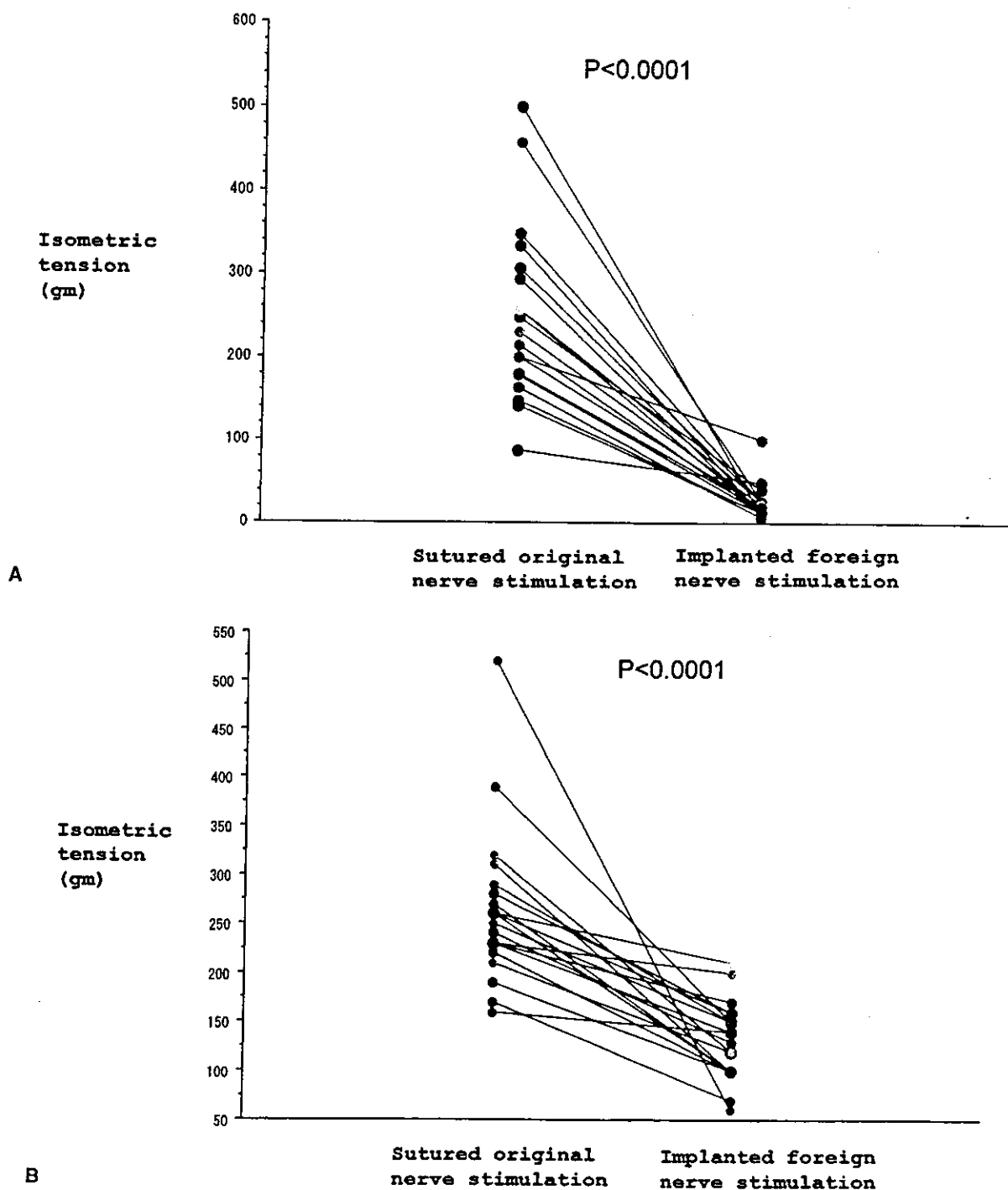


Figure 3 Plot of isometric tension for sutured original nerve stimulation and implanted foreign nerve stimulation. (A) Nerve suture group. (B) Nerve graft group.

nerve-graft group (Fig. 2B). This appeared to preclude a preventive effect in the nerve-graft group.

Comparison of isometric tension in response to stimulation of the implanted nerve and that caused by stimulation of the repaired nerve on the direct neurotization side showed that the former was 12.6 ± 14.4 percent (mean \pm S.D.) of the latter in the suture group (Fig. 3A) and 50.9 ± 16.9 percent of the latter in the graft group (Fig. 3B). On the direct neurotization side,

tension evoked by stimulation of the implanted nerve was 131.5 ± 39.2 gm in the nerve-graft group and 24.6 ± 20.8 gm in the nerve-suture group ($p < 0.0001$). Thus, reinnervation by the implanted nerve was more active in the nerve-graft group than in the nerve-suture group.

Histologically, larger muscle fiber diameter on the direct neurotization side was confirmed in both the nerve-suture (Fig. 4A) and the nerve-graft groups

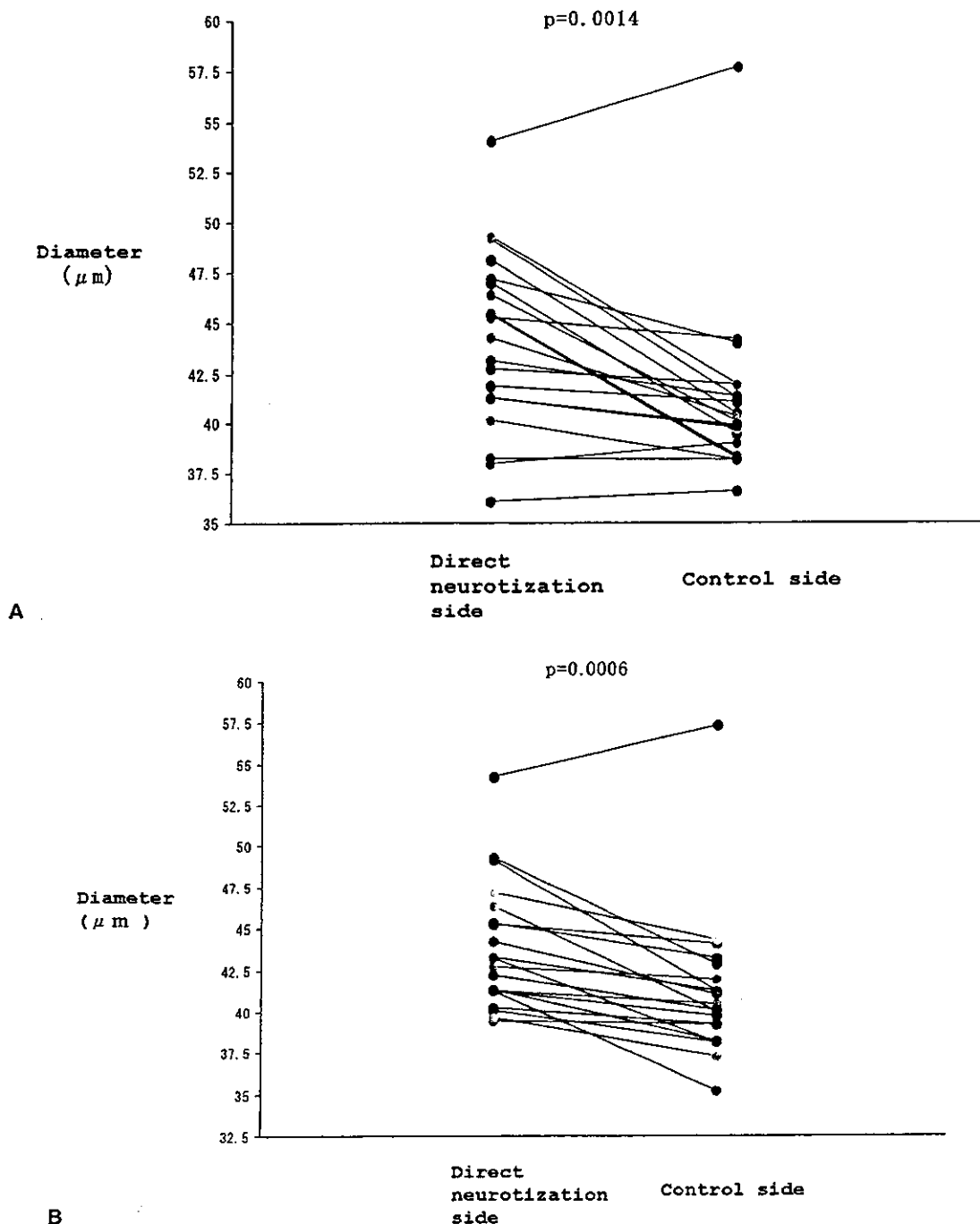


Figure 4 Plot of gastrocnemius muscle fiber mean diameter on the direct neurotization side and the control side. (A) Nerve suture group. (B) nerve graft group.

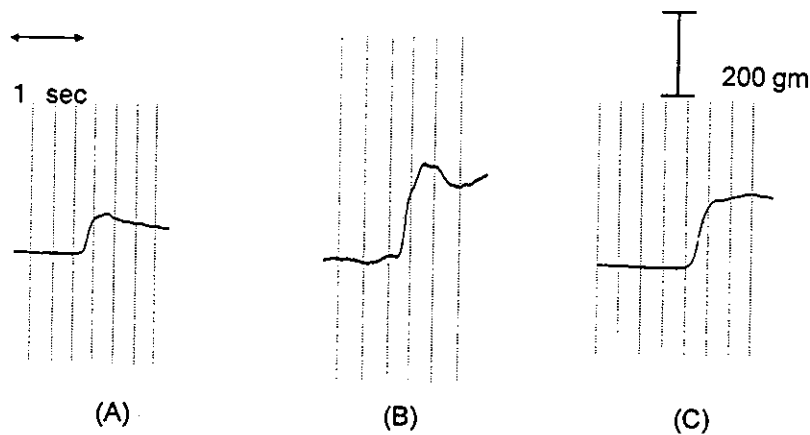


Figure 5 Example of isometric tension measurement in one animal in the nerve suture group. (A) Sutured original nerve stimulation (direct neurotization side). (B) Implanted foreign nerve stimulation (direct neurotization side). (C) Sutured original nerve stimulation (control side).

(Fig. 4B). Results from one animal in the nerve-suture group are shown in Figures 5-7.

DISCUSSION

Direct neurotization, as well as neural and muscular neurotization, are established modes of reinnervation with a history that dates back to 1914.⁹ Numerous studies have clarified the properties and mechanism of direct neurotization,¹⁰⁻²⁰ and clinically successful results have been reported for several methods of nerve implantation.²¹⁻²³ The degree of functional recovery in response to direct neurotization is of great interest from a clinical standpoint, because it will determine whether this technique can be used in a babysitter procedure.

Several studies have provided evidence in favor of the use of direct neurotization. Sakellarides et al.¹³ reported that contractility induced by direct neurotization averaged 60 to 75 percent that of normal innervated muscle in a dog model. Mochida⁷ reported contractility of 68 percent that of the normal contralateral muscle 52 weeks after direct neurotization when the nerve was

implanted near the motor point (proximal direct neurotization), whereas contractility was 42 percent that of the normal contralateral muscle when implantation was at the endplate-free zone (distal direct neurotization), and approximately 75 percent that of normal muscle after neural neurotization. At a 6-month follow-up, Frey et al.²⁴ reported tension recovery of 62.2 percent of normal by proximal direct neurotization and 84.5 percent of normal by neural neurotization. According to Kijima et al.,⁸ 24 weeks after implantation, a 56.6 percent recovery rate occurred in response to proximal direct innervation, a 40.2 percent recovery rate occurred in response to distal direct neurotization, and an 88.4 percent recovery rate occurred in response to neural neurotization.

The intensity of muscle contraction appears to differ according to the site of implantation. These differences may be related to the property of the endplate, that is, whether a new endplate or a preexisting endplate is involved. In direct neurotization, two processes of muscle reinnervation occur: one forms a new endplate, and the other uses a preexisting endplate.²⁵⁻²⁷ Generally, when the nerve is implanted far from the



Figure 6 Gastrocnemius muscle taken for histologic evaluation after tension measurement from the same animal as in Figure 5. Left: Direct neurotization side (muscle weight 1.80 gm). Right: Control side (muscle weight 1.22 gm).

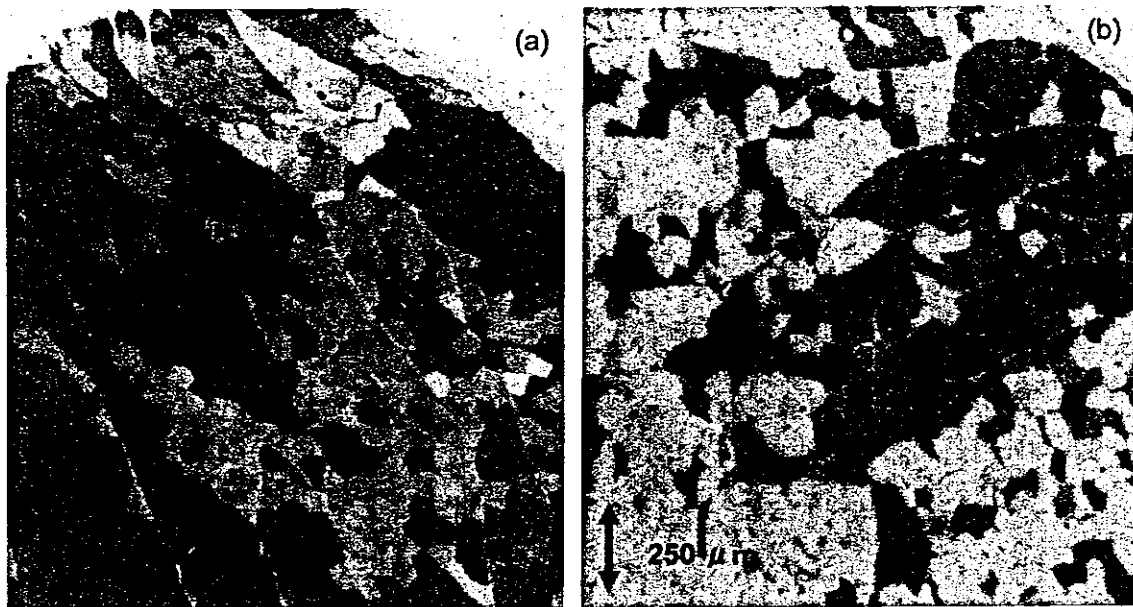


Figure 7 Cross section of gastrocnemius muscle stained for ATPase, preincubated at pH 4.4, from the same animal as in Figure 5. (a) Direct neurotization side (mean muscle fiber diameter 48 μm). (b) Control side (mean muscle fiber diameter 42 μm).

motor point, the former process predominates, whereas when the nerve is implanted near the motor point, the latter process predominates. Preexisting endplates appear to be superior to new endplates in function; thus, proximal direct neurotization is more effective than distal direct neurotization. Therefore, to obtain the best muscle function in response to direct neurotization, the nerve should be implanted near the motor point.

To be useful in a babysitter procedure, reinnervation by direct nerve implantation must progress rapidly. Fex and Theslef¹¹ observed the first muscle twitch on the twelfth day after nerve implantation, and Morioka²⁸ confirmed the accumulation of Ach-E activity beginning 1 week after nerve implantation. Similarly, other studies of direct neurotization have shown early initiation of muscle contraction (3 to 6 weeks,⁶ 4 weeks⁸), although procedural details and materials differ. These studies show that the implanted nerve has considerable ability as a motor source, indicating that it may be useful as a babysitter.

To evaluate the effectiveness of direct neurotization for the prevention of denervation atrophy, we must also consider the interaction between direct and neural neurotization. Even if the muscle fiber is reinnervated by the implanted foreign nerve, the muscle must be able to accept further reinnervation by the original nerve. Only when this is possible can denervation atrophy be minimized.

Two types of interaction occur between two nerves innervating the same target: coexistence and exclusion. Coexistence allows double innervation by the two nerve fibers, and exclusion involves the suppression of innervation of one nerve by the other. Controversy exists concerning double innervation. Muscle

fibers innervated by two nerve fibers have been observed morphologically,^{1,10} but it is unclear whether both synapses are functional. While Frank et al.²⁹ observed a high rate of functional double innervation in a rat model, Gutmann and Young¹ concluded that the endplate in rabbits is reinnervated by only one nerve branch and observed that when a large and a small nerve fiber approach a plate, only the former innervates it. Similarly, Kijima et al.⁸ concluded from electrophysiologic study of two nerves implanted to the same muscle that one functioning muscle fiber did not possess two functioning endplates. McArdle³⁰ suggested that mammalian muscle fibers are multiply innervated during the early stages of reinnervation, and Rotshenker and McMahan³¹ reported that such multiple reinnervation lasts only 7 months in the frog. Generally, double innervation appears to be rare in mature muscle fibers. Therefore, the idea of suppression of one nerve by another predominates. Although Frank et al.²⁹ disagree, reinnervation by the original nerve is assumed to suppress the function of foreign synapses.³²⁻³⁴

Given the model of suppression, we interpret our results as follows. In the nerve-suture group, the muscle fibers are reinnervated initially by the implanted nerve, replaced later by the repaired nerve. Denervation atrophy, which usually occurs until reinnervation by the repaired original nerve, is prevented, resulting in relatively high isometric muscle tension when the repaired original nerve is stimulated and in low isometric muscle tension when the implanted nerve is stimulated. In the nerve-graft group, where reinnervation by the repaired nerve is delayed, the change from innervation by the implanted nerve to that by the repaired nerve does not progress well. The neuromuscular junction, which

belongs to the implanted nerve, becomes stable and does not relinquish innervation to the regenerated axons of the repaired nerve. Therefore, the isometric tension of the muscle remains low when the repaired original nerve is stimulated and is relatively high when the implanted nerve is stimulated. In both groups, early reinnervation through the implanted nerve occurs and prevents denervation atrophy, regardless of whether the type of innervation changes or not, resulting in a larger muscle diameter on the direct neurotization side in both groups.

Our results show that a relatively short interval between direct neurotization by an implanted nerve and reinnervation by the repaired original nerve promotes the success of the babysitter procedure. In clinical applications, however, this procedure should be effective even when neural neurotization by the original nerve is delayed for long periods, which would cause severe denervation atrophy of the muscle. To obtain a clinically satisfactory babysitter effect by direct nerve implantation, it may be necessary to resect the implanted nerve early, after reinnervation by the original nerve commences.

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特集 頭頸部癌の治療指針—私たちはこうしている—

4. 下咽頭癌の治療 —切除範囲と再建—

3) 上部消化管との重複癌症例の再建

岡崎 睦* 朝戸裕貴** 多久嶋亮彦** 中塚貴志***
波利井清紀**

I. はじめに

下咽頭癌は早期発見が難しく頭頸部癌の中でも予後が悪い疾患であり、食道癌との合併率が高いことが知られている。林ら¹⁾は、国立がんセンター中央病院および東病院頭頸科において、原発巣切除術を行った下咽頭癌未治療例 120 例中 17 例 (14%) に食道癌を認めたと報告している。また吉積ら²⁾は、下咽頭癌手術症例における胸部食道癌合併率が、同時・異時合わせて 6%であったと報告している。

近年では、下咽頭癌の患者に対してルゴール液塗布による術前食道内視鏡スクリーニング検査がルーチン化され、早期食道癌の発見率が上昇してきた。合併する食道癌に対する治療としては、内視鏡的粘膜切除 (EMR)、非開胸食道全摘 (食道抜去)、開胸食道全摘などが行われている。食道癌が粘膜内癌であれば EMR で治療できる可能性は高く、下咽頭癌に対する再建のみで食道癌の再建は必要としない。しかし、食道癌が粘膜を超えて浸潤している場合は、下咽頭喉頭頸部食道切除術 (以下、咽喉食摘術と略す) に加えて食道を全摘することになり、下咽頭から全食道の再建が必要になる。下咽頭・頸部食道癌に対する標準的な咽喉

食摘術後の再建術式としては、現在では遊離空腸移植術が主流である^{3,4)}。一方、胸部食道癌に対する再建術式では、胃管、大腸、小腸による再建が症例に応じて用いられているが、これら単独では咽頭喉頭食道全摘術後の長大な欠損に対する再建は難しく、再建できたとしても再建食道末梢の血行が不安定で、部分壊死や瘻孔形成を生じる危険性が高いため、再建にも工夫が必要である。

本稿では、癌の発生部位や浸潤度に対する適切な切除術式やリンパ節郭清については成書に譲ることとし、下咽頭・頸部食道と上部消化管との重複癌の切除後に生じた消化管の欠損に対してわれわれが行っている再建方法について述べたい。

II. 切除範囲と再建材料の決定

われわれの施設では、下咽頭癌に対する再建術式として遊離空腸移植を第 1 選択としており^{3,4)}、標準的な咽喉食摘術に対しては、通常の管状遊離空腸移植で再建している。前腕皮弁などの皮弁を用いる再建は、縫合する距離が長く 3 点縫合部を生じるため、術後に瘻孔を生じる危険性が高く³⁾、また遊離空腸を用いた再建のほうが粘膜同士の縫合になるため、創傷治癒も早く術後縫合不全の頻度が低いと考えられるからである。喉頭温存手術などの部分的な咽頭粘膜欠損に対しては、パッチ状に遊離空腸移植を行い再建しているが、皮弁を用いた再建でも 3 点縫合部が生じないため、前腕皮弁による再建も適応があると考えている。

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表 1 下咽頭・頸部食道癌と胸部食道癌の同時性重複癌の再建

1) 胃管が使用可能な場合
胃管による再建 (頸部血管に supercharge)
胃管のみでは咽頭断端に届かない場合
咽頭：胃管間に遊離空腸を間置 (消化液の逆流防止効果もあり)
2) 胃管が使用不可能な場合 (胃癌の重複, 過去に胃潰瘍の手術など)
(1) 結腸が使用可能な場合
右半結腸もしくは回結腸の吊り上げ移植 (頸部血管に supercharge)
回結腸が咽頭断端に到達できない場合
咽頭：回結腸間に遊離空腸を間置
(2) 結腸が使用不可能な場合 (結腸癌の重複, 既往など)
① 有茎空腸 (胸部または頸部の血管に 2 組の supercharge が必要な場合もある)
② 2 segments 遊離空腸移植 (胸部, 頸部の血管へ 2 組の血管吻合)

下咽頭・頸部食道癌と重複する上部消化管癌の部位では胸部食道と胃があるが、胃癌との重複では、基本的にはそれぞれの癌に対してそれぞれの切除再建術を行うことになるので、臨床上消化管欠損の再建が問題になるのは胸部食道癌との重複である。下咽頭・頸部食道と胸部食道の重複癌では、消化管欠損は中咽頭以下の全食道となる。この広範囲の欠損に対しては、通常胸部食道癌の再建に準じて、胃・小腸・大腸などの残された消化管を用いて再建を行うが、単独の材料では再建が不可能な場合は、それらの材料を組み合わせて再建を行うことになる。通常胸部食道癌の再建術式では咽頭断端まで到達できないか、たとえ物理的に到達したとしても遠位部の部分壊死や縫合不全の可能性は高くなると考えられる。それらの合併症が生じた場合、長期間の経口食事摂取が不能になり、また周囲組織の炎症その他の悪条件を伴う非常に困難な二次再建が必要になるため、即時再建で、なるべく安全かつ確実な再建法を選択することが重要であると考えられる。

重複癌は同時性と異時性とに分けられるが、異時性でも基本的には同時性の場合に準ずる再建方法となる場合が多いので、まずは同時性重複癌について詳しく述べ、異時性重複癌について追加したいと思う。

1. 下咽頭癌・頸部食道癌と胸部食道癌の同時性重複癌 (表 1)

(1) 胃管の使用が可能な場合は、まず胃管による再建を考える。再建の必要な範囲が高位に及び、その分胃管の血行に不安が生じるため、胃管遠位

部の血管と頸部血管との間に血管吻合 (supercharge) を行うことを原則とする。胃管の吊り上げは通常、右胃大網動静脈を血管茎として行われるので、この場合、右胃大網動静脈と交通をもつ左胃大網動静脈、短胃動静脈または脾動静脈を吻合血管として用いる。移植床の頸部血管としては、動脈は上甲状腺動脈や頸横動脈 (端々吻合)、静脈は内頸静脈 (端側吻合) を用いることが多い。胃管の挙上だけでは咽頭断端に到達できない場合は遊離空腸移植を間置する。遊離空腸の間置は、胃管から消化液の逆流を防止する効果もある⁵⁾。空腸を間置せずに延長胃管を形成して、左胃動脈を頸部血管と吻合する再建法もあるが⁶⁾、延長胃管の遠位部が部分壊死に陥る症例も報告されている⁷⁾。再建食道の部分壊死後の二次再建は困難な場合が多いので、われわれは通常胃管の遠位血管を supercharge し、症例により遊離空腸を間置する再建法のほうが安全であると考えている。

(2) 胃管の使用が不可能な場合 (胃癌が重複する、以前に胃潰瘍や胃癌などにより胃が既に切除されている場合など) は、順行性の右半結腸や回結腸の吊り上げを用いて再建する。この場合は中結腸動静脈を血管茎として挙上し、回結腸動静脈を内胸動静脈または頸部血管に supercharge するのが原則とする。咽頭断端に到達できない場合は、胃管での再建と同様に、咽頭断端との間に遊離空腸を間置する⁸⁾。この再建方法では、通常は胸骨前経路が用いられるが、われわれは胸骨後経路を好んで採用している。このほうが短経路となり、その分安全な血行が確保できると考えられるから