Table 7 Occurrence of Thrombosis (1990~1999)

Postoperative Days	Total n=76	Artery n=38	Vein n=38
Within 24 hrs	42 (55.3%)	17 (44.7%)	25 (65.8%)
2 days	9 (11.8%)	7 (18.4%)	2 (5.3%)
3 days	10 (13.2%)	7 (18.4%)	3 (7.9%)
((Within 3 days	61 (80.2%)	31 (81.6%)	30 (79.0%))
More than 3 days	9 (11.8%)	3 (7.9%)	6 (15.8%)
Unknown	6	4	2

tive pressure. These factors act favorably in preventing thrombus formation. Many lower extremity defects result from trauma or chronic infection, leading to limitation of available healthy recipient vessels.

Although microvascular anastomosis in elderly patients seems difficult because of higher rates of vascular degeneration, such as intimal thickening or atherosclerotic change, no evident increase in flap necrosis and thrombus formation was observed in our series, compared to those of the younger generation. As some authors have reported,[16,17] age itself is not a contraindication for free flap transfer.

Reports of flap salvage rate following exploration range from 33 to 78 percent,[18–21] while we observed a salvage rate of 56.0 percent in our series. Venous thrombosis resulted in a significantly higher salvage rate, in comparison to arterial thrombosis. This is mainly because it is easier to detect venous thrombosis clinically with conventional monitoring methods, and venous congestion can be compensated for by bleeding from the flap margin for a while before progressing to a non-reparable situation.

Vascular occlusion by thrombus formation resulting from some technical failure or inappropriate choice of recipient vessels usually occurs in the early postoperative period. We think that late thrombosis (which occurs more than 3 days after surgery) results mainly from local infection subsequent to fistula formation, or mechanical stress around the anastomotic site, rather than the above-mentioned causes. Therefore, one must carefully observe the wound for at least 1 week after operation.

Table 8 Postoperative Complications (Other Than Flap Necrosis and Vascular Thrombus)

Major fistulae*	79
Infection	122
Bleeding	26
Local skin necrosis	21
Hematoma	8
Ileus	8
Lymphorrhea	7
Others	49

*fistulae which required surgical intervention for closure

In conclusion, our clinical experience showed that three conventional free flaps (the rectus, forearm, and jejunum) still constitute major elements in the armamentarium of head and neck reconstruction, and have maintained better flap survival rates compared to other flaps. The recent introduction of more sophisticated flaps, such as perforator-based flaps and primarily thinned flaps, widens free flap application as well as offering improved cosmetic results with less donor-site morbidity. However, these latter flaps demand a sophisticated level of skill and experience. Furthermore, judicious flap selection is fundamental for sustaining a stable and predictable success rate for cancer patients.

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Endoscopic dissection of recipient facial nerve for vascularized muscle transfer in the treatment of facial paralysis

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SUMMARY. In order to prepare recipient facial nerve branches for neurovascular muscle, transfer in the treatment of facial paralysis, endoscopic facial nerve dissection was employed. Under endoscopy recipient facial nerve branches innervating the zygomaticus major muscle were successfully dissected. A stab incision was sufficient for nerve suture with the donor nerve. This method is preferable for young or female patients in whom conventional cheek incisions should be avoided. © 2003 The British Association of Plastic Surgeons. Published by Elsevier Science Ltd. All rights reserved.

Keywords: facial paralysis, neurovascular free muscle transfer, facial nerve, endoscopy.

Surgical reconstruction of facial paralysis remains challenging, despite various techniques devised to recover facial expression. Since Harii et al[1] first reported the use of neurovascular free gracilis muscle transfer for treating long-standing facial paralysis, many reconstructive surgeons have preferentially used this method.[2–7] A two-stage method combining free muscle transfer with cross-face nerve graft has long been popularized and preferred,[8–10] but a one-stage free muscle transfer in which the muscle motor nerve directly crosses through the face has also been developed.[11–15]

Compared to the two-stage method combined with cross-face nerve grafting, the one-stage method offers advantages including a shorter recovery period and no need for harvesting the sural nerve. However, the length of the muscle motor nerve is limited and not long enough to reach a contralateral pre-auricular incision. Thus, an incision on the intact cheek is required to expose recipient facial nerve branches and link them to the motor nerve of the transferred muscle. Although such cheek scarring is largely inconspicuous among elderly patients,[9] scarring on the non-paralyzed cheek can represent an annoyance, particularly for children and young women.

To avoid such morbidities during one-stage free muscle transfer, we developed an endoscopic technique for dissecting recipient facial nerve branches through small pre-auricular incisions. Using this endoscopic technique, facial nerve branches suitable as a recipient motor source are accurately dissected, and a small stab incision to the cheek is sufficient to allow the facial and grafted motor nerves to be sutured under microscopy. Even after developing this endoscopic dissection technique, we still appreciate conventional recipient facial nerve dissection through a small incision, about 2 cm long,[11] at the anterior region of the parotid gland as a first choice. However, we consider this novel technique an option worthy of consideration for young or female patients.

Presented at the 42nd Annual Meeting of the Japan Society of Plastic and Reconstructive Surgery, Fukuoka, Japan, in April 1999.

Operative technique

After creating a subcutaneous pocket for subsequent muscle transfer in the paralyzed cheek, two incisions of about 1 cm each in length are placed on the pre-auricular region of the non-paralyzed side (Fig. 1). From each incision, the superficial musculoaponeurotic system (SMAS) plane is dissected blind, anterior to the intercross point of the inferior edge of the zygomatic arch and the anterior margin of the parotid gland. The two incisions are thus connected subcutaneously. After the right-handed surgeon introduces an endoscope (30° angle, 4 mm diameter, 17.5 cm long) through the left incision, dissection is continued using a microdissector inserted through the right incision. In cases where sufficient optic space cannot be attained, the pre-auricular skin is hooked and lifted, or adjunctive traction of the cheek skin is performed using 3–0 silk thread (Fig. 2). Dissection proceeding anteriorly under video assistance enables visualization of several facial nerve branches at the anterior margin of the parotid gland. Among these branches, those innervating the zygomaticus major muscle can be found by dissecting the undersurface of this muscle (Fig. 3).

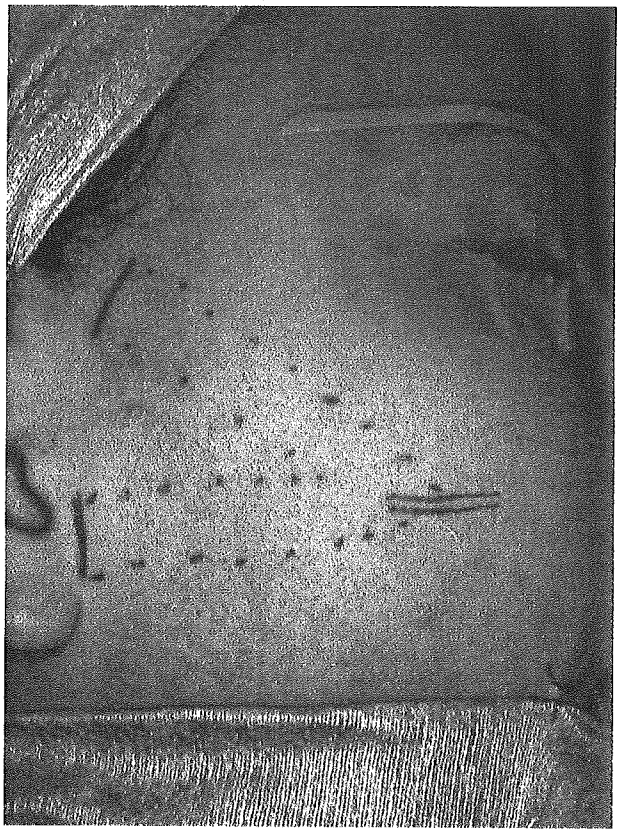

Fig. 1—Two incisions are placed on the pre-auricular region of the non-paralyzed side. From each incision, the SMAS plane is dissected blind as the dotted lines indicate.

After dissecting these branches proximally and distally as far as possible, a small stab incision is created on the non-paralyzed cheek to pull out the stump of these facial nerve branches. In order to pull out these branches sufficiently, the stab incision should be made parallel to the nerve about 2 cm proximal to the point at which the branches are severed. When the stab incision is created just above the nerve stumps, pulling out a sufficient length of nerve stump for subsequent microsurgical nerve suture to the muscle motor nerve stump is impossible. Vessel tape is inserted from this stab incision to bind around and retract the nerve from the incision. Recipient facial nerve branches are then severed as far distally as possible (Fig. 4), followed by removing the vessel tape to bring the nerve stumps outside the stab incision (Figs 5 and 6). After setting the harvested neurovascular muscle segment into the recipient cheek pocket, the muscle motor nerve is passed through the upper lip using a specially designed nerve passer, then pulled out from the same stab incision. The muscle motor nerve and selected recipient facial nerve branches are then joined epineurally under a microscope using 10–0 monofilament nylon sutures. Finally, the sutured nerves are reintroduced into the subcutaneous space, followed by confirmation of nerve suturing under endoscopy. Compression dressing on the non-paralyzed cheek is not required.

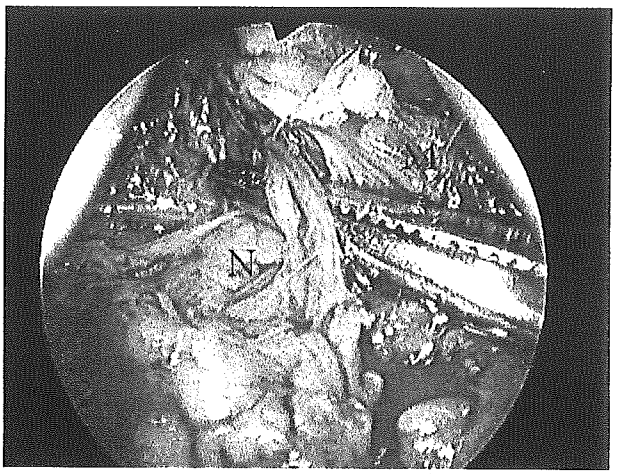

Fig. 3—Endoscopic dissection enables visualization of several facial nerve branches. Among these branches, those innervating the zygomaticus major muscle can be found by dissecting the undersurface of this muscle. M: zygomaticus major muscle, N: facial nerve branch.

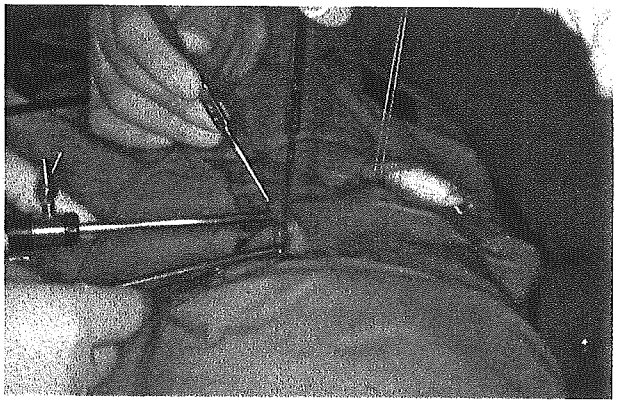

Fig. 2—After the right-handed surgeon introduces an endoscope through the left incision, dissection is continued using a microdissector inserted through the right incision. The pre-auricular skin is hooked, and adjunctive traction of the cheek skin is performed using 3–0 silk thread, since sufficient optic space cannot be attained.

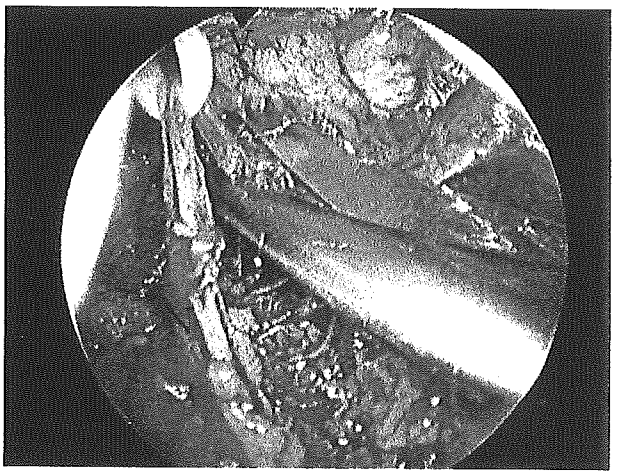

Fig. 4—Recipient facial nerve branches are severed as far distally as possible. V: vessel tape, N: facial nerve branch.

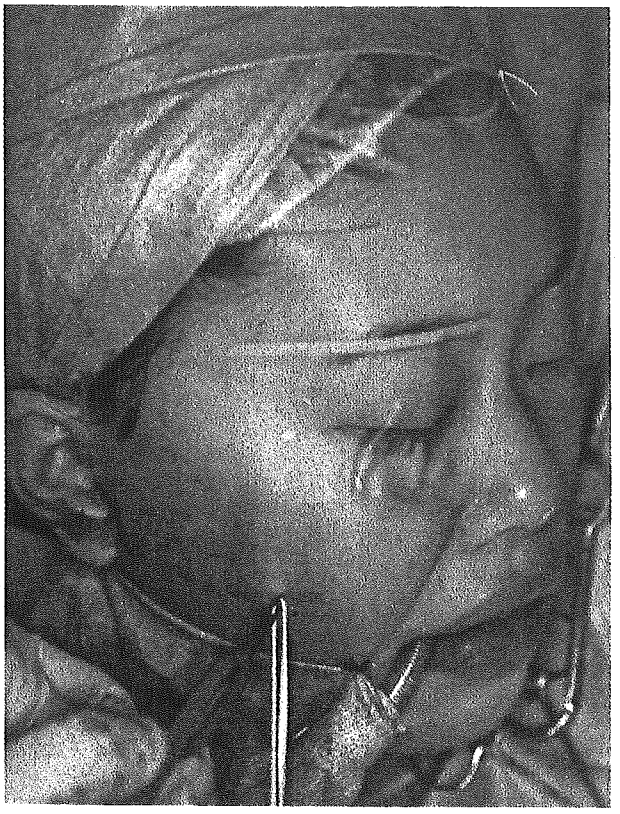

Fig. 5—The vessel tape is removed to bring the nerve stumps.

Results

Endoscopic facial nerve dissection was performed on 8 patients (7 females, 1 male) who underwent one-staged facial paralysis reconstruction using the latissimus dorsi muscle (Table I). Patients ranged in age from 15- to 50-years-old (mean, 32.1-years-old) at time of surgery. Morbidities causing the facial paralysis are listed in Table I. Ancillary procedures accompanying muscle transfers comprised gold plate loading in the upper eyelid of patients 1 and 8, temporal muscle transfer to the eyelid of patients 2 and 5, and endoscopic eyebrow lift for patients 2, 5, and 8.

Mean duration of endoscopic facial nerve dissection was 34 min, ranging from 30 to 50 min. Muscle contraction was confirmed in all patients between 4 and 9 months postoperatively, to ensure that the endoscopic procedure had not damaged recipient nerves. Cheek scars were imperceptible in all patients (Fig. 7).

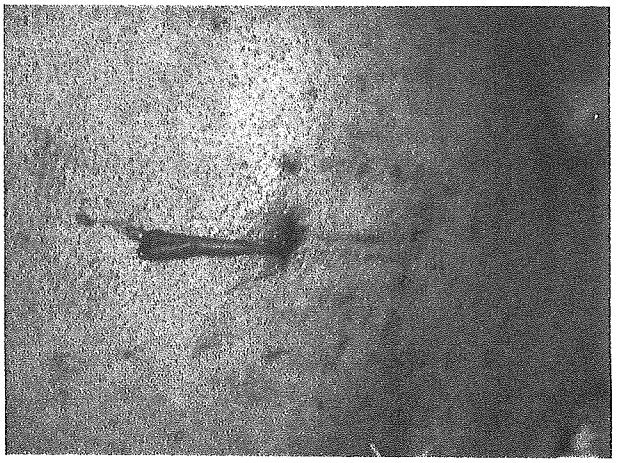

Fig. 6—The stump of the recipient facial nerve branches are brought outside the stab incision.

Discussion

Since the aim of microvascular free muscle transfer is the reconstruction of a synchronous natural smile, the facial nerve branches innervating the zygomatic and levator labii muscles on the contralateral side should be selected as recipient motor nerves. Suitable branches of the facial nerve can be identified through either a pre-auricular face-lift incision or a small incision placed on the intact cheek. According to Manktelow et al,[16] the pre-auricular approach is preferable because it allows more accurate identification of all nerve branches and their functions through the use of a nerve stimulator. In this method, since sufficient sural nerve can be harvested to cross the face and reach the contralateral pre-auricular region, nerve suture between the sural nerve and recipient facial nerve can be performed under microscopy from the pre-auricular incision. The pre-auricular incision method may be useful when the two-stage operation combining muscle transfer with cross-face nerve grafting is selected. However, when the one stage muscle transfer is employed, nerve suture from the pre-auricular incision is almost impossible even though the incision extends anteriorly over the mandibular angle. This is because the length of the motor nerve of donor muscles is not long enough to reach the contralateral pre-auricular region. For this reason, most authors who report one-stage free muscle transfer use an incision placed on the cheek for nerve juncture.[11,13,14] According to Kumar,[15] most female patients and children in his series

Table I Patient data

Patient	*Age*	*Sex*	*Original disease*	*Paralyzed side*	*Time (min) for endoscopy*	*Initial contraction (pom)*	*Anicillary procedures*
1	38	F	Parotid tumor	lt.	50	5	LL
2	38	F	Acoustic neurinoma	rt.	40	6	EEL, TT
3	25	F	Bell's palsy	rt.	30	5	
4	15	F	Neck tumor	lt.	30	5	
5	50	F	Acoustic neurinoma	lt.	30	6	EEL, TT
6	37	M	Bell's palsy	rt.	30	9	
7	28	F	Acoustic neurinoma	rt.	30	7	
8	26	F	Otitis media	rt.	30	4	EEL, LL

pom, postoperative months; EEL, endoscopic eye-brow lift; LL, lid load with a gold plate; TT, temporal muscle transfer to the eyelid.

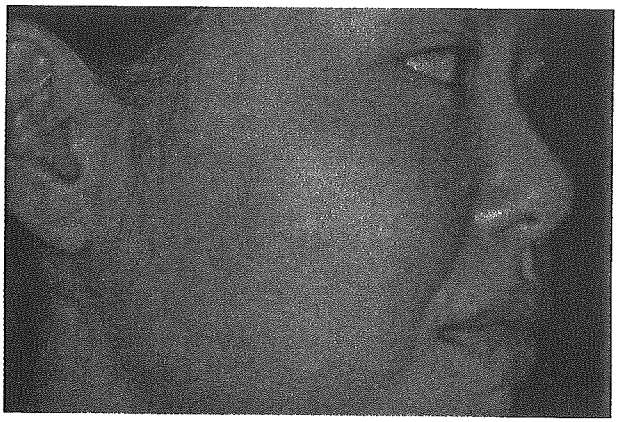

Fig. 7—Pre-auricular and cheek scars were imperceptible.

preferred the two-stage procedure to avoid scarring of the cheek on the intact side. In order to address this problem, we attempted a technique using endoscopic facial nerve dissection enabling nerve suture through a stab incision on the cheek.

Compared to the pre-auricular or cheek incision methods, endoscopic facial nerve dissection cannot assure nerve selection using the nerve stimulator. However, control of the nerve stimulator requires experience, and contraction of the upper lip orbicularis oris can be misinterpreted as that of the levator and zygomaticus muscles.[16] Conversely, nerve branches selected as recipient for muscle transfer can be clearly identified under endoscopic magnification as innervating the zygomaticus major muscle.

Generally, the benefits of surgical endoscopy include enhanced visualization, fewer and smaller incisions, and reduced iatrogenic morbidity compared to conventional approaches. However, our endoscopic technique requires more skin incisions and the area of subcutaneous dissection needed for endoscopic visualization is larger than that of the cheek approach, although the method is still less invasive than the pre-auricular approach. This technique is, therefore, not indicated for senile patients in whom skin incisions on the cheek are always inconspicuous. An endoscopic approach is indicated for young female patients who prefer two pre-auricular skin incisions to a larger incision on the cheek, for cosmetic reasons.

The time required for endoscopic procedures is another problem for both physicians and patients. Even with technical improvements, endoscopic facial nerve dissection required at least 30 min. Conversely, conventional nerve dissection from a cheek incision requires 10–15 min on average. However, facial preparation, including endoscopic facial nerve dissection, can be performed while the neurovascular muscle flap is harvested. The time required for endoscopic procedure, therefore, does not represent a major problem.

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Craniofacial Surgery for Malignant Skull Base Tumors

Report of an International Collaborative Study

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BACKGROUND. Malignant tumors of the skull base are rare. Therefore, no single center treats enough patients to accumulate significant numbers for meaningful analysis of outcomes after craniofacial surgery (CFS). The current report was based on a large cohort that was analyzed retrospectively by an International Collaborative Study Group.

METHODS. One thousand three hundred seven patients who underwent CFS in 17 institutions were analyzable for outcome. The median age was 54 years (range, 1–98 years). Definitive treatment prior to CFS had been administered in 59% of patients and included radiotherapy in 367 patients (28%), chemotherapy in 151 patients (12%), and surgery in 523 patients (40%). The majority of tumors (87%) involved the anterior cranial fossa. Squamous cell carcinoma (29%) and adenocarcinoma (16%) were the most common histologic types. The margins of surgical resection were reported close/positive in 412 patients (32%). Adjuvant postoperative radiotherapy was received by 510 patients (39%), and chemotherapy was received by 57 patients (4%).

RESULTS. Postoperative complications were reported in 433 patients (33%), with local wound complications the most common (18%). The postoperative mortality rate was 4%. With a median follow-up of 25 months, the 5-year overall, disease-specific, and recurrence-free survival rates were 54%, 60%, and 53%, respectively. The histology of the primary tumor, its intracranial extent, and the status of surgical margins were independent predictors of overall, disease-specific, and recurrence-free survival on multivariate analysis.

CONCLUSIONS. CFS is a safe and effective treatment option for patients with malignant tumors of the skull base. The histology of the primary tumor, its intracranial extent, and the status of surgical margins are independent determinants of outcome. ***Cancer* 2003;98:1179–87.** *© 2003 American Cancer Society.*

KEYWORDS: skull base neoplasms/surgery, postoperative complications, skull base neoplasms/mortality, treatment outcome, international cooperation.

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The combined transfacial and transcranial surgical approach for resection of tumors of the skull base has evolved considerably since its original description.[1-3] Advances in neuroradiologic imaging, combined with improved surgical technique, the availability of microvascular reconstructive options, and the realization of the importance of multidisciplinary collaboration,have contributed to the widespread acceptance of craniofacial surgery (CFS) as a preferred treatment option for patients with tumors of the skull base. In modern practice, CFS is performed for a variety of histologic types, both benign and malignant. However, because of the relative rarity of these problems, no single center treats enough patients to accumulate significant numbers for meaningful analysis of outcomes. To overcome these difficulties, an International Collaborative Study Group comprised of 17 institutions was set up to report their collective experience with the objective of assessing the safety and efficacy of CFS based on a large patient cohort. The major purpose of this endeavor was to establish a benchmark against which the results of other approaches and future treatment strategies may be assessed. The current report is an overview of the results of this collaborative effort.

MATERIALS AND METHODS

A multi-item questionnaire was sent to all participating investigators to obtain information on patients, tumors, treatment variables, and outcomes of treatment. Data were collected retrospectively. Completed data sheets on patients treated between October 1956 and January 2000 were submitted by each investigator to the central analyzing office for data entry, compilation, and statistical analysis.

Data Entry, Patient Exclusions, and Statistical Methods

Data were entered into a commercially available spreadsheet (Microsoft Excel 2000; Microsoft Corporation, Redmond, WA), and statistical analysis was performed using computerized software packages (JMP Version 4.0; SAS Institute, Cary, NC, and SPSS for Windows, Version 11.01; SPSS, Chicago, IL). The total number of patients submitted by the 17 contributors was 1541 (range, 13–205; median, 73 per investigator). Of these, 114 patients had to be excluded because information on either pathology (n = 26) or outcome data (n = 88) were not available. After these exclusions, a total of 1427 patients were eligible for analysis. Of the 1427 analyzable patients, 120 had benign tumors and were excluded from this analysis. Therefore, this report on CFS for patients with malignant tumors was based on the remaining 1307 patients.

The follow-up interval was calculated in months from the date of CFS to the date of last follow-up or death, and the recurrence-free interval was calculated from the recorded date of CFS to the date of first recurrence. For disease-specific survival, patients who reportedly died of nondisease-related causes (111 of 1307 patients; 8.5%) and patients who were alive with disease at last follow-up (109 of 1307 patients; 8.3%) were censored. Overall survival, disease-specific survival, and recurrence-free survival rates were calculated using the Kaplan–Meier method and univariate comparisons of survival were performed using the log-rank test. A P value ≤ 0.05 was considered significant, and all significant factors were entered into a multivariate analysis using the Cox proportional hazards model. Nonparametric qualitative and quantitative comparisons were performed using the Fisher exact or Pearson chi-square tests and the Mann–Whitney U test, respectively.

TABLE 1
Patient Demographics

Characteristic	No. of patients (%)
Age group (yrs)	
< 20	81 (6.2)
21–40	224 (17.1)
41–70	811 (62.0)
> 70	149 (11.4)
Data not reported	44 (3.2)
Gender	
Male	848 (64.9)
Female	428 (32.7)
Data not reported	31 (2.4)
Medical comorbidity	
None	1010 (77.3)
Present	170 (13.0)
Data not reported	127 (9.7)
Karnofsky performance score	
< 50%	3 (0.2)
50–75%	59 (4.6)
> 75%	1113 (85.2)
Data not reported	132 (10.0)

Patient Demographics

Patients ranged in age from 1 year to 98 years, with a median age of 54 years. Table 1 presents the demographic data on these patients.

Primary Tumor

The anatomic attributes and extent of the primary tumors are listed in Table 2. Squamous cell carcinoma and adenocarcinoma were the most common histologic variants. Due to heterogeneity in reporting, meaningful analysis of the individual categories of TNM staging was not possible. Stage grouping, how-

TABLE 2
Location, Extent, and Pathology of the Primary Tumor

Feature	No. of patients (%)
Location of the primary tumor at the skull base	
Anterior cranial fossa	1136 (86.9)
Middle cranial fossa	127 (9.7)
Anterior and middle cranial fossa	44 (3.4)
Orbital invasion	
None	540 (41.3)
Periosteum	137 (10.5)
Bone	322 (24.6)
Intraorbital contents	294 (22.5)
Data not reported	14 (1.1)
Intracranial extension	
None	540 (41.3)
Bone invasion	387 (29.6)
Dural invasion	282 (21.6)
Brain invasion	84 (6.4)
Data not reported	14 (1.1)
Cranial nerve deficits	
None	1019 (78.0)
Present	271 (20.7)
Data not reported	17 (1.3)
Skin invasion	
None	998 (76.4)
Present	293 (22.4)
Data not reported	16 (1.2)
TNM stage grouping	
Stage I	27 (2.0)
Stage II	72 (5.5)
Stage III	136 (10.4)
Stage IV	610 (46.7)
Data not reported	462 (35.4)
Pathology	
Adenocarcinoma	210 (16.1)
Esthesioneuroblastoma	151 (11.6)
Melanoma	53 (4.1)
Other malignancies	89 (6.8)
Malignant salivary tumors	124 (9.5)
High-grade sarcoma	93 (7.1)
Low-grade sarcoma	53 (4.1)
Squamous cell carcinoma	375 (28.8)
Skin malignancies	120 (9.1)
Undifferentiated or anaplastic tumors	39 (3.0)

ever, was reported in 845 patients (64.7%); and, among these, 746 patients (88.3%) presented with Stage III or IV disease.

Treatment

Most patients had undergone some form of treatment prior to CFS (Table 3). The dose of previous radiotherapy was available for 311 patients (84.8%), and it ranged from 480 centigrays (cGy) to 9000 cGy, with a median of 5950 cGy; 27 patients (7%) received reirradiation after undergoing CFS. Three patients (0.2%) had been treated previously with brachytherapy.

Table 4 lists the details of CFS, reconstruction, and

TABLE 3
Details of Treatment Administered before Craniofacial Surgery[a]

Treatment	No. of patients (%)
Prior treatment	
No	535 (40.9)
Yes	765 (58.5)
Data not reported	3 (0.2)
Previous surgery	
No	781 (59.8)
Yes	523 (40.0)
Data not reported	3 (0.2)
Previous radiotherapy	
No	929 (71.1)
Yes	367 (28.1)
Data not reported	11 (0.8)
Previous chemotherapy	
No	1144 (87.5)
Yes	151 (11.6)
Data not reported	12 (0.9)

[a] Of 248 patients, 19% were treated with more than 1 modality.

margin status. Adjuvant postoperative radiotherapy (PORT) was administered in 39% patients, with a median dose of 6000 cGy (range, 1440–6200 cGy). Adjuvant brachytherapy was used for only 3 patients, whereas 57 patients (4.4%) were treated with adjuvant chemotherapy (Table 5).

Follow-Up

The follow-up interval ranged from 1 month to 940 months, with a median of 25 months. Follow-up was > 5 years in 310 patients (23.7%).

RESULTS

Overall, it was recorded that one-third of patients developed postoperative complications. Information on postoperative complications was not available for 114 patients (8.7%). The most common complications were related to the local wound, whereas the postoperative mortality rate was 4.3% (Table 6). The presence of medical comorbid conditions, prior treatment with radiotherapy, and the intracranial extent of the tumor were associated significantly with the development of postoperative complications. Patient age and the presence of comorbid conditions were significant predictors of postoperative mortality (data not shown).

With a median follow-up of 25 months (range, 1–940 months), the 5-year overall survival and disease-specific survival rates calculated using the Kaplan–Meier method were 53.6% and 59.9%, respectively (Fig. 1). Recurrent disease after CFS was recorded in 545 patients (41.7%). The recurrence-free interval was not available for analysis in 54

TABLE 4
Details of Craniofacial Resection

Feature	No. of patients (%)
Type of approach	
Anterior fossa	988 (75.6)
Middle fossa	94 (7.2)
Anterior and middle fossa	81 (6.2)
Data not reported	144 (11.0)
Extent of resection (data available for 589 patients)	
Orbit	207 (35.1)
Maxilla	246 (41.8)
Nasal cavity, other sinuses	138 (23.4)
Craniofacial bones	86 (14.6)
Skin	53 (9.0)
Brain	6 (1.0)
Infratemporal fossa contents	23 (3.9)
Margins of surgical resection	
Close	191 (14.6)
Negative	710 (54.3)
Positive	221 (17.0)
Data not reported	185 (14.1)
Tracheostomy	
No	869 (66.5)
Yes	287 (22.0)
Data not reported	151 (11.5)
Reconstruction	
No	143 (11.0)
Yes	1028 (78.6)
Data not reported	136 (10.4)
Type of reconstruction (n = 1028)	
Autologous nonvascularized tissue	163 (15.9)
Cadaveric or bovine tissue	10 (1.0)
Free flaps	222 (21.6)
Locoregional flaps	594 (57.8)
Multiple flaps	6 (0.6)
Nonvascularized bone	21 (2.0)
Titanium mesh	12 (1.2)

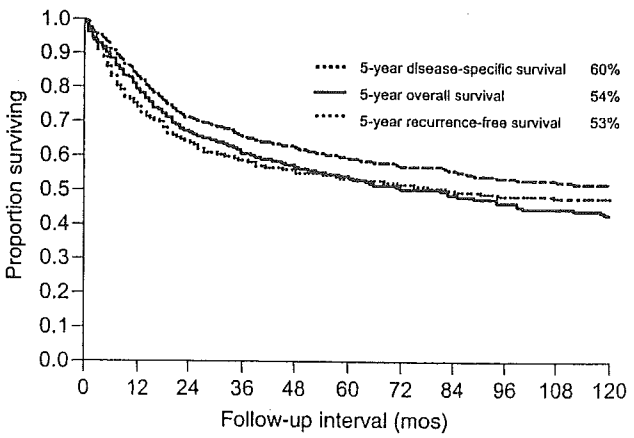

FIGURE 1. Survival outcomes after craniofacial surgery for patients with malignant skull base tumors.

TABLE 5
Adjuvant Treatment

Treatment	No. of patients (%)
Adjuvant radiotherapy	
No	766 (58.6)
Yes	510 (39.0)
Data not reported	31 (2.4)
Adjuvant brachytherapy	
No	1267 (97.0)
Yes	3 (0.2)
Data not reported	37 (2.8)
Adjuvant chemotherapy	
No	1219 (93.3)
Yes	57 (4.4)
Data not reported	31 (2.4)

TABLE 6
Postoperative Complications after Craniofacial Resection

Type of complication	No. of patients (%)
Complications	
No	760 (58.2)
Yes	433 (33.1)
Data not reported	114 (8.7)
Wound complications	
No	956 (73.2)
Yes	237 (18.1)
Data not reported	114 (8.7)
Central nervous system complications	
No	1000 (76.5)
Yes	193 (14.8)
Data not reported	114 (8.7)
Systemic complications	
No	1136 (86.9)
Yes	57 (4.4)
Data not reported	114 (8.7)
Orbital complications	
No	1173 (89.7)
Yes	20 (1.5)
Data not reported	114 (8.7)
Postoperative mortality	
No	1137 (87.0)
Yes	56 (4.3)
Data not reported	114 (8.7)

patients (4.1%). The median time to recurrence was 19 months (range, 1–940 months), and the 5-year recurrence-free survival rate was 52.8%. The histology of the primary tumor, the extent of intracranial extension, and the status of surgical margins were independently significant predictors of recurrence-free survival (Table 7) and disease-specific survival (Table 8). In addition to these factors, the presence of medical comorbidity predicted worse overall survival (Table 9).

TABLE 7
Prognostic Predictors of Recurrence-Free Survival

Covariate	No. of patients	5 yr RFS (%)	Univariate analysis (log-rank test)	Multivariate analysis	
				RR	95% CI
Age (yrs)					
≤ 50	523	53.4	0.9		
> 50	742	52.8			
Gender					
Female	428	51.4	0.2		
Male	828	54.2			
Medical comorbidity					
None	1007	50.3	0.6		
Present	170	53.2			
Anatomic location					
Anterior cranial fossa	1136	55.7			
Middle cranial fossa	127	34.1			
Both	44	37.3	< 0.0001[a]	NS	
Orbital involvement					
None	540	58.9			
Periosteum/bone	459	51.1			
Intraorbital contents	294	43.7	< 0.0001[a]	NS	
Intracranial involvement					
None	540	62.1		Reference	
Bone	387	56.3		0.9	0.7–1.2
Dura	282	39.5		1.4	1.1–1.8
Brain	84	20.9	< 0.0001[a]	1.9	1.3–2.7[b]
Histology					
Esthesioneuroblastoma	151	64.3		Reference	
Skin malignancies	120	60.1		1.1	0.7–1.8
Low-grade sarcomas	53	62.6		1.9	1.0–3.5
Other malignancies	89	61.2		1.6	0.9–2.8
High-grade sarcomas	93	52.2		1.6	1.0–2.6
Adenocarcinoma	210	53.1		2.1	1.5–3.1
Salivary malignancies	124	44.3		1.6	1.1–2.5
Squamous cell carcinoma	375	49.9		1.8	1.2–2.5
Undifferentiated/anaplastic carcinoma	38	45.5		6.0	3.7–9.8
Mucosal melanomas	53	19.2	< 0.0001[a]	11.1	6.4–19.5[b]
Surgical margins					
Negative	710	64.1		Reference	
Positive	412	29.6	< 0.0001[a]	2.3	1.8–2.9[b]
Previous radiotherapy					
No	929	56.3		Reference	
Yes	367	43.5	< 0.0001[a]	1.7	1.4–2.1[b]
Previous chemotherapy					
No	1144	54.4			
Yes	151	41.1	0.002[a]	NS	

RFS: recurrence-free survival; RR: relative risk; 95% CI: 95% confidence interval; NS: not significant.
[a] Statistically significant.
[b] $P < 0.0001$ (statistically significant).

DISCUSSION

The current study was based on information on the largest number of patients accumulated in a single report on the subject. The objective of the study was to establish an international benchmark for outcomes after CFS for patients with skull base tumors. The obvious advantage of such a collaborative approach is that a larger population of patients becomes available for analysis; however, it may be argued that the study population is heterogenous, because these patients were treated at different institutions spread over many different continents. However, the institutions that participated in the current collaborative study practice skull base surgery on a sufficiently regular basis to have attained a standard of excellence in the field. Although the basic CFS technique may not differ sig-

TABLE 8
Prognostic Factors for Disease-Specific Survival

Covariate	No. of patients	5 yr DSS (%)	Univariate analysis (log-rank test)	Multivariate analysis	
				RR	95% CI
Age (yrs)					
≤ 50	523	60.0			
> 50	742	60.4	0.5		
Gender					
Female	428	58.0			
Male	828	61.2	0.5		
Medical comorbidity					
None	1007	60.2			
Present	170	59.3	0.8		
Anatomic location					
Anterior cranial fossa	1136	61.9			
Middle cranial fossa	127	47.1			
Both	44	42.9	0.0009[a]	NS	
Orbital involvement					
None	540	66.2			
Periosteum/bone	459	59.2			
Intraorbital contents	294	48.2	0.0004[a]	NS	
Intracranial involvement					
None	540	66.0		Reference	
Bone	387	60.7		1.0	0.8–1.4
Dura	282	53.6		1.4	1.0–1.9
Brain	84	29.3	< 0.0001[a]	2.1	1.4–3.1[b]
Histology					
Esthesioneuroblastoma	151	82.6		Reference	
Skin malignancies	120	74.9		1.5	0.8–2.7
Low-grade sarcomas	53	74.0		2.6	1.3–5.5
Other malignancies	89	68.7		2.0	1.0–4.0
High-grade sarcomas	93	58.7		2.6	1.5–4.5
Adenocarcinoma	210	57.5		3.0	1.9–4.8
Salivary malignancies	124	53.0		2.0	1.1–3.4
Squamous cell carcinoma	375	53.0		2.7	1.7–4.2
Undifferentiated/anaplastic carcinoma	39	41.9		2.8	1.4–5.5
Mucosal melanomas	53	19.2	< 0.0001[a]	11.1	6.4–19.5[b]
Surgical margins					
Negative	710	73.5		Reference	
Positive	412	37.8	< 0.0001[a]	2.3	1.8–2.9[b]
Previous radiotherapy					
No	929	63.7		Reference	
Yes	367	50.2	< 0.0001[a]	1.8	1.4–2.2[b]
Previous chemotherapy					
No	1144	61.5			
Yes	151	46.8	0.002[a]	NS	

DSS: disease-specific survival; RR: relative risk; 95% CI: 95% confidence interval; NS: not significant.
[a] Statistically significant.
[b] $P < 0.0001$ (statistically significant).

nificantly from institution to institution, the indications for CFS and adjuvant therapy may vary according to the institutional practice. A collaborative analysis such as the current one allows assessment of the role of CFS in the management of skull base tumors amidst institutional variations. Nonetheless, heterogeneity in data collection and reporting may undermine the usefulness of such collaborations. In collating and analyzing data for this study, it was evident that significant improvements are needed to optimize the quality and uniformity of reporting certain patient and tumor-related variables.

The overwhelming majority of patients who require CFS have locally advanced tumors. It is not uncommon for these patients to have undergone limited surgical manipulation and/or nonsurgical treat-

TABLE 9
Prognostic Factors for Overall Survival

Covariate	No. of patients	5 yr OS (%)	Univariate analysis (log-rank test)	Multivariate analysis RR	Multivariate analysis 95% CI
Age (yrs)					
≤ 50	523	57.1	0.08		
> 50	742	51.2			
Gender					
Female	428	51.6	0.8		
Male	828	55.0			
Medical comorbidity					
None	1007	55.3	0.03[a]	Reference	
Present	170	43.6		1.3	1.0–1.6[b]
Anatomic location					
Anterior cranial fossa	1136	55.8			
Middle cranial fossa	127	38.9			
Both	44	40.2	0.0002[a]	NS	
Orbital involvement					
None	540	61.1			
Periosteum/bone	459	52.4			
Intraorbital contents	294	41.5	< 0.0001[a]	NS	
Intracranial involvement					
None	540	62.0		Reference	
Bone	387	51.9		1.1	0.9–1.5
Dura	282	46.8		1.4	1.1–1.8
Brain	84	23.2	< 0.0001[a]	2.1	1.4–3.0[c]
Histology					
Esthesioneuroblastoma	151	77.8		Reference	
Skin malignancies	120	71.0		1.9	1.2–3.2
Low-grade sarcomas	53	68.9		2.2	1.1–4.3
Other malignancies	89	62.6		1.9	1.0–3.6
High-grade sarcomas	93	57.4		2.4	1.4–3.9
Adenocarcinoma	210	51.5		2.9	1.9–4.4
Salivary malignancies	124	45.5		2.1	1.3–3.4
Squamous cell carcinoma	375	44.4		2.7	1.8–4.0
Undifferentiated/anaplastic carcinoma	39	37.3		2.8	1.6–5.1
Mucosal melanomas	53	18.3	< 0.0001[a]	8.8	5.3–14.7[c]
Surgical margins					
Negative	710	65.7		Reference	
Positive	412	32.8	< 0.0001[a]	2.3	1.8–2.9[c]
Previous radiotherapy					
No	929	57.8		Reference	
Yes	367	43.3	< 0.0001[a]	1.6	1.3–1.9[c]
Previous chemotherapy					
No	1144	55.0			
Yes	151	42.0	0.02[a]	NS	

OS: overall survival; RR: relative risk; 95% CI: 95% confidence interval; NS: not significant.
[a] Statistically significant.
[b] $P < 0.05$ (statistically significant).
[c] $P < 0.0001$ (statistically significant).

ment prior to referral to a skull base surgical unit. This is reflected in the fact that almost 60% of the patients in the current study had undergone some form of prior treatment for their tumors. Along with an awareness of the safety and efficacy of CFS, it is crucial for physicians treating patients with tumors of the skull base to be aware of the indications and limitations of nonsurgical modalities so that the appropriate treatment is made available to these patients without undue delay. In addition, anatomic localization and staging of the tumor is more difficult for the skull base surgeon when confronted with a patient whose tumor has been manipulated prior to referral. This may have contributed to the findings that the majority of pa-

tients in the current study did not have information available on the exact anatomic subsite of origin and that the TNM stage grouping was not reported in 35% of patients.

Tumors of the nasal cavity or paranasal sinuses invading the anterior skull base constitute the most common indication for CFS in modern practice, and this is evident in the distribution of anterior CFS relative to other approaches reported in this study. The technique of CFS and its variations have been well described in the literature.[4,5] Over the past few decades, there has been increasing awareness that autologous vascularized tissue generally is superior to other reconstructive options. This is especially true with the advent and widespread availability of microvascular tissue transfer. Most authors are in agreement that a pedicled galeal-pericranial flap is ideal for reconstructing the anterior central skull base after routine CFS, whereas microvascular flaps are suitable for more extensive defects of the anterior and middle fossa.

The importance of *histologically* complete resection of malignant tumors in improving the ultimate outcome cannot be overemphasized. The current analysis shows that patients who have close or positive margins have significantly worse outcomes compared with patients who have surgical resection margins that are free of tumor. Although the impact of monobloc resection of tumors has not been examined systematically (and, for obvious reasons, will never be examined systematically), there can be little doubt that piecemeal resection or *debulking* of tumors is more likely to be associated with positive margins of resection. It is therefore important to reiterate that, when feasible, the skull base surgeon should strive to achieve a monobloc resection of the tumor with negative margins of resection.

Like the current study, most individual series of CFS with significant numbers have reported postoperative complications in approximately one-third of patients.[6–21] Although complication rates after CFS seem high, the postoperative mortality rate has remained under 5% for the past 2 decades. The indications for CFS have expanded progressively over the years commensurate with advances in neuroradiologic assessment, surgical and reconstructive techniques, and perioperative care. Consequently, modern skull base surgeons are more willing to resect locally advanced tumors even in patients who have significant comorbid medical conditions. Despite this, the postoperative mortality rate in the current collaborative study was only 4%. Similar figures have been reported in other major individual series.[6–21] The role of comorbid medical conditions and the extent of the primary tumor in the treatment algorithm may appear intuitive, but the relative impact of these variables on outcome after CFS is demonstrated vividly by our data. Patients who have comorbid medical problems and tumor extending intracranially into the brain are significantly more likely to develop postoperative complications. Similarly, an increased risk of postoperative complications was noted in patients who had been treated previously with external beam radiotherapy. This may be attributed to treatment selection bias, because primary radiation therapy may be prescribed more likely for patients who have associated medical comorbid conditions and patients with larger tumors that are believed to be *unresectable.* Although the retrospective nature of our analysis precluded the determination of any conclusive cause-and-effect relation, the adverse effect of prior radiation therapy on both postoperative recovery and survival outcome is noteworthy. It may be appropriate to emphasize here that successful treatment of a patient with a malignant skull base tumor requires appropriate treatment selection through the combined efforts of a multidisciplinary team; and, for most patients who are both physiologically eligible and technically suitable for the procedure, CFS is a safe and effective primary treatment option. The majority of complications are related to local wound problems, whereas orbital and systemic morbidity is less common. These complications generally resolve with conservative management and do not cause undue prolongation of postoperative recovery. However, it is important to realize that successful outcome after CFS is directly related not only to the technical expertise of the surgical team, but equally to the quality of perioperative and rehabilitative care.

The addition of PORT is accepted as standard practice for patients with locoregionally advanced malignant tumors of the head and neck. The threshold for the addition of PORT to the treatment plan generally is lower in patients undergoing CFS because of the inherent anatomic difficulty in obtaining wide surgical margins of clearance. Adjuvant PORT was administered to 39% of patients in the current study, and this figure may have been limited by the fact that as many as 28% of patients had been treated with external beam radiation therapy prior to referral for CFS. Although the impact of PORT probably will never be examined in a prospective, randomized fashion, it is worth noting that disease-specific survival rates for patients who were treated with PORT approached the rates for patients who did not require PORT. The implication of this observation, albeit in the retrospective setting, is that comparable outcomes could be achieved in patients who had more advanced tumors

and thus may have been selected for PORT. In contrast, the role of chemotherapy in the management of skull base tumors is less defined. There are individual institutional reports of the use of concurrent chemoradiation in the management of surgically unresectable tumors of the skull base, but these will need verification on a larger (preferably multiinstitutional) scale.[22]

The overall survival and disease-specific survival rates reported in the current collaborative study were comparable to those reported in the literature.[6–21] Our data demonstrate that the overall survival rate was influenced significantly by the presence of comorbid medical conditions. This trade-off seems inevitable, because improvements in perioperative management have expanded the criteria for patient selection. Tumor-related variables, such as the histologic type and extent of intracranial involvement, influence overall, disease-specific, and recurrence-free survival. Patients with certain tumors, such as esthesioneuroblastoma and skin malignancies, have better outcomes independent of other factors, whereas patients with melanoma or undifferentiated/anaplastic tumors inevitably fare worse. Similarly, intracranial extension of the tumor that involves the brain is a significantly adverse prognostic indicator. Finally, the ability to achieve complete resection of the tumor with negative surgical margins significantly influences all outcome parameters. These prognostic predictors, therefore, should be factored into treatment planning for patients with tumors that appear technically to be resectable using a craniofacial approach.

In conclusion, combined transfacial and transcranial surgical resection is a safe and effective treatment option for patients with malignant tumors of the skull base. The histology of the primary tumor, its intracranial extent, and the status of surgical margins are independent predictors of recurrence-free survival, overall survival, and disease-specific survival.

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ALTERNATIVE APPROACH USING THE COMBINED TECHNIQUE OF NERVE CROSSOVER AND CROSS-NERVE GRAFTING FOR REANIMATION OF FACIAL PALSY

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An alternative approach, using a combination of nerve crossover and cross-nerve grafting technique in a single-stage procedure, was developed for the reconstruction of reversible facial palsy. This combined technique provides some benefits such as early facial reanimation resulting from the single-stage procedure, less morbidity and sufficient innervation with an application of the end-to-side anastomosis method, and efficient neural regeneration due to coaptation of the intratemporal facial nerve. Facial nerve rehabilitation, based on double innervation by hypoglossal and contralateral healthy facial nerves, takes advantage of reliable and physiological facial reanimation.

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The value of nerve crossover and cross-face nerve grafting has become widely accepted for early facial reanimation following proximal facial nerve injury near the brain stem. These techniques to reanimate the paralyzed face are generally used when there is no considerable atrophy of the mimetic muscles within 12–24 months from the onset of facial palsy.

With the nerve crossover technique, rapid restoration of resting tone and powerful facial movements of the reinnervated face are obtained.[1,2] Currently, hypoglossal-facial nerve neurorrhaphy, with some modifications to reduce the damage to the hypoglossal nerve and avoid postoperative hemiglossal dysfunction, has become the most popular nerve crossover method.[3–7] On the other hand, with cross-face nerve grafting, coordinated facial motion is provided due to the use of the contralateral facial nerve as a motor source. This technique refers to an interpositional graft of the sural nerve placed between the facial nerve branches of the healthy side and corresponding facial nerve branches on the paralyzed side.[8,9] Recently, there have been some reports on the two-stage facial reanimation procedure, which is a combination of hypoglossal nerve crossover and cross-face nerve grafting to obtain more effective and physiological results.[10–12]

This article reports on an alternative approach for early facial reanimation, using a combination of nerve crossover and cross-nerve grafting techniques in a single-stage procedure.

CASE REPORT

A 68-year-old man underwent resection of an acoustic tumor, which resulted in a total facial palsy on the right side (Fig. 1). Facial nerve reconstruction, in combination with nerve crossover and cross-nerve grafting technique, was carried out 3 months after neurosurgery. This reanimation surgery was planned in a single-stage procedure with the cooperation of the plastic surgical and neurosurgical teams.

In the nerve crossover procedure, following a postauricular incision extended downward along the anterior margin of the sternocleidomastoid muscle and submandibular region, the mastoid process was partially resected to open the stylomastoid foramen. The descending portion of the facial nerve in the mastoid

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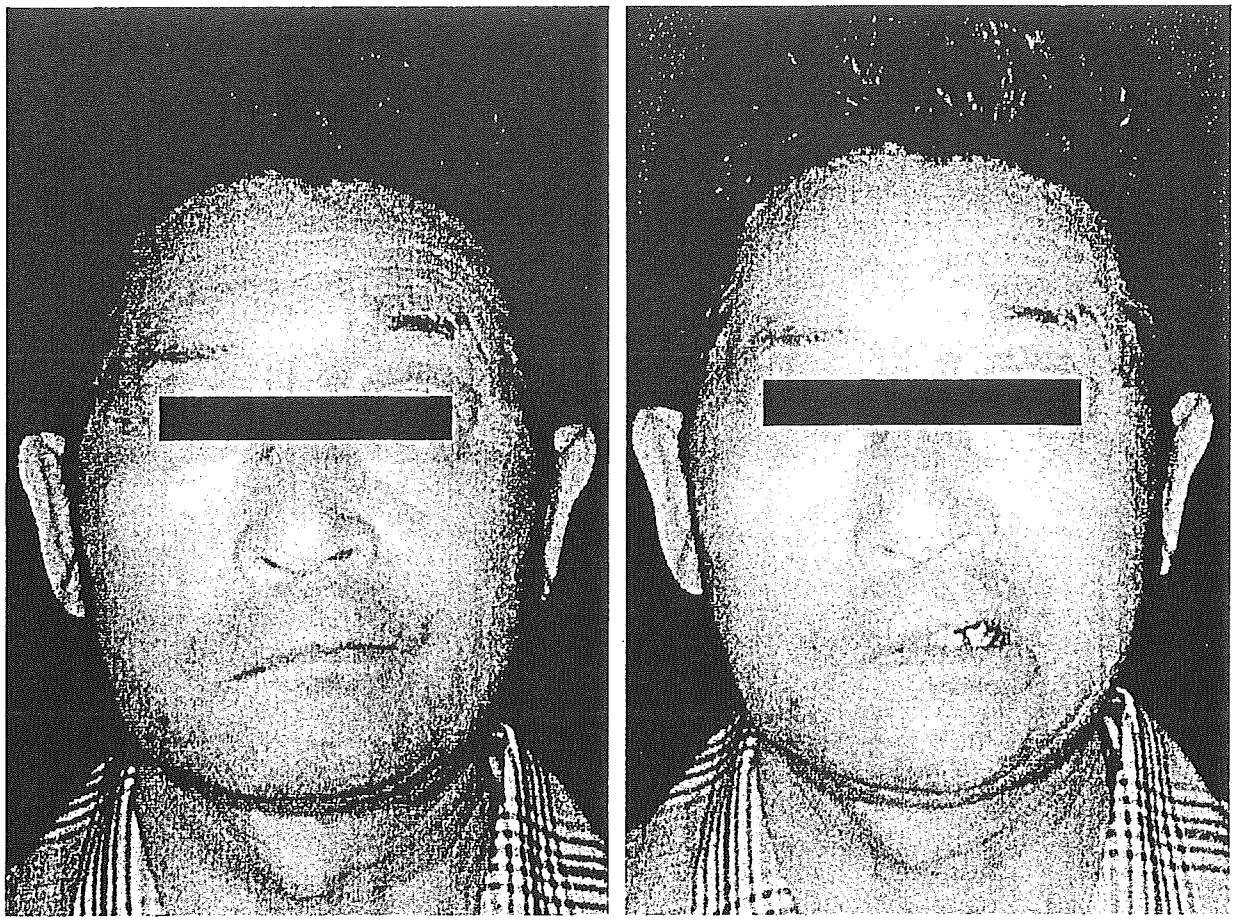


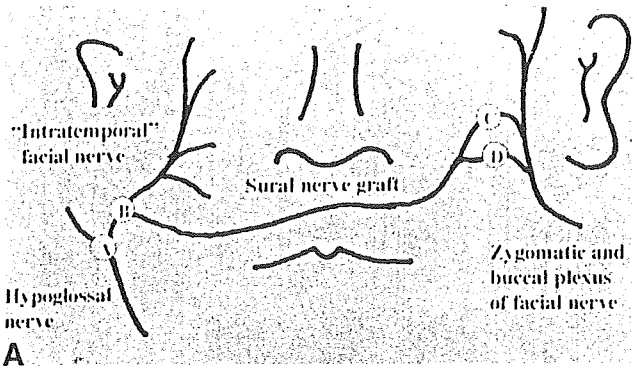
A B

*Figure 1. Preoperative appearance. **A:** At rest. **B:** Smiling.*

cavity, which was the "intratemporal facial nerve," was exposed over 3 cm in length and transected. The distal stump of the intratemporal facial nerve was mobilized down into the submandibular region. Then the hypoglossal nerve beneath the internal jugular vein was exposed, with retraction of the posterior belly of the digastric muscle to the inferoposterior direction. Under the operating microscope, 40–50% partial neurectomy was made on the lateral surface of the hypoglossal nerve, where the mobilized intratemporal facial nerve could be touched without any tension. Side-to-end neurorrhaphy was carried out between the neurectomy site of the hypoglossal nerve and the distal stump of the intratemporal facial nerve. Assisting sutures were also placed into the connective tissues surrounding these nerves, to further reduce tension on this neural tissue anastomosis.

In the cross-face nerve grafting procedure, two normal branches of the zygomatic and buccal plexus of the facial nerve were identified through two small skin incisions medial to the parotid gland on the normal side. A 28-cm-long sural nerve graft was tunneled across the upper lip and brought to the mandibular angle region. Then the epineural window on the paralyzed facial nerve trunk was created just lateral to the parotid gland by removal of the epineural sheath. End-to-side neurorrhaphy was carried out between the end of the nerve graft and the main trunk of the facial nerve through the epineural window. The other end of the nerve graft was divided into two fascicles and connected to the identified zygomatic and buccal branches of the healthy facial nerve without tension (Fig. 2).

The signs of mimetic muscle recovery started at 9 months after surgery, and facial reanimation progressively improved during the follow-up period. At postoperative month 13, an upper blepharoplasty was added on the palsy side at the patient's request. Currently, 22 months have passed; the patient has regained sufficient facial muscle tone and synchronous mimetic movement. At smiling, contraction of the reinnervated orbicularis oculi muscle was noted in the lateral canthal region. Also, the nasolabial fold at the reconstructed side was



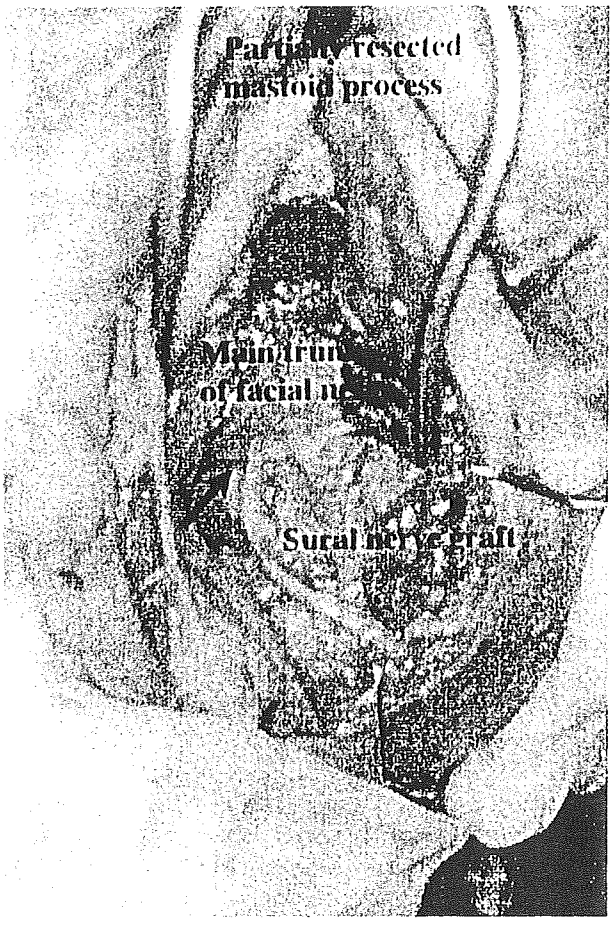


Figure 2. ***A:*** *Schematic drawing of authors' approach, using a combination of nerve crossover and cross-nerve grafting techniques in single-stage procedure. Neurorrhapy A, side-to-end anastomosis between neurectomy site of hypoglossal nerve and distal stump of intratemporal facial nerve; neurorrhapy B, end-to-side anastomosis between end of sural nerve graft and main trunk of facial nerve through epineural window; neurorrhapy C and D, end-to-end anastomoses between two fascicles of nerve graft and zygomatic and buccal branches of healthy facial nerve.* ***B:*** *Intraoperative view of end-to-side anastomosis between end of sural nerve graft and main trunk of facial nerve through epineural window. Arrow indicates neurorrhapy site.*

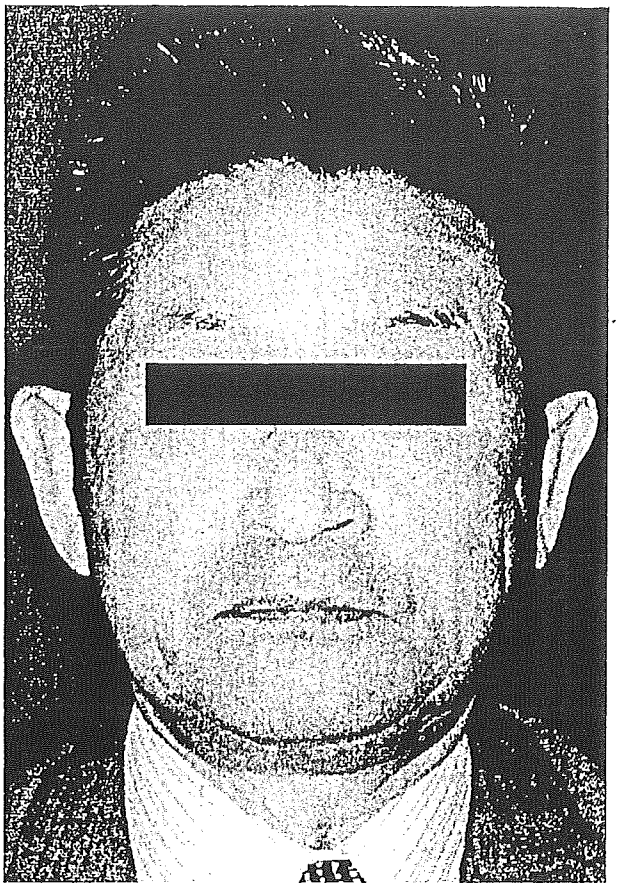


Figure 3.

furrowed by contraction of the reinnervated zygomatic major muscle. He exhibited almost complete restoration of facial symmetry, without hemiglossal dysfunction (Fig. 3).

Electroneuromyographic (ENMG) evaluation was performed 18 months after surgery. ENMG studies, with stimulation of the hypoglossal nerve on the paralyzed side and the facial nerve on the normal side, showed double innervation of the peripalpebral and perioral muscles on the operated side. Action potentials of these reinnervated mimetic muscles were noted by stimulation of the hypoglossal nerve and contralateral facial nerve through the cross-face nerve grafting (Fig. 4).

DISCUSSION

The hypoglossal nerve and the contralateral facial nerve are the most utilized motor donors in the treatment of reversible facial palsy when there is no atrophy of the facial mimetic muscles. Although the hypoglossal-facial nerve crossover technique provides reliable restoration

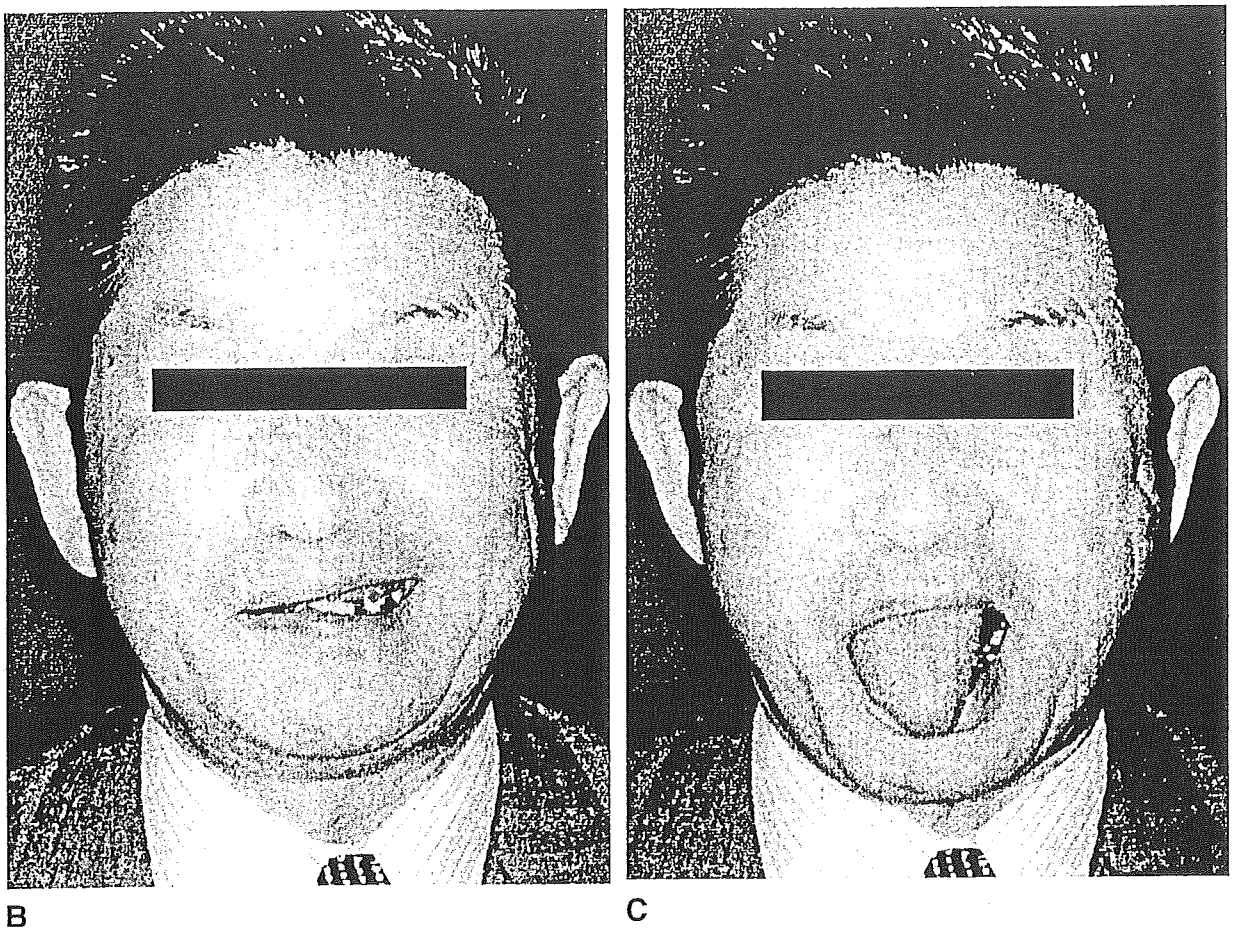


Figure 3. Continued.
*Figure 3. Appearance 20 months postoperatively. **A:** At rest. **B:** Smiling. **C:** No clear evidence of tongue atrophy.*

of facial movement, this procedure leads to hemiglossal dysfunction, resulting in talking, chewing, and swallowing difficulties. To solve these problems, the hypoglossal-facial nerve side-to-end anastomosis method, involving approximately 40% partial neurectomy or removal of epi/perineurium of the hypoglossal nerve, has been developed.[3,5–7] In these techniques, some modifications such as interposing a nerve graft or mobilization of the distal part of the intratemporal facial nerve was necessary to obtain a tensionless anastomosis (Table 1). However, the nerve crossover method is associated with undesirable movement in the reanimated mimetic muscles. Therefore, the cross-face nerve grafting method, in which the contralateral healthy facial nerve provides a new source of innervation, is superior in terms of coordinated movement of the reinnervated face.

To obtain more physiological facial recovery, a combined technique with hypoglossal nerve crossover and cross-face nerve grafting has been introduced.[10–12] This technique is also aimed at preventing irreversible atrophic change of the paralyzed mimetic muscles during the long regeneration time of neural axons through cross-face nerve grafting. This combined technique was achieved in two stages in previous publications. The hypoglossal-facial nerve crossover and sural crossed facial nerve graft are carried out in the first stage. Eleven to 20 months later, in the second stage, distal ends of the cross-facial nerve graft are coapted with the peripheral branches of the facial nerve on the paralyzed side (see Table 1).

The authors' approach, using the combined technique of nerve crossover and cross-nerve grafting, involved some modifications compared to previous reports. First, the present technique was carried out in a single-stage procedure. The main disadvantages of the two-stage procedure are the delay between stages and the burden on patients undergoing multiple surgeries. In 1994, Inigo et al. demonstrated favorable results of recovery of facial palsy in patients undergoing single-stage cross-facial nerve grafting less than 1 year after the onset of facial palsy.[13] Although there is controversy in the single-stage achievement of cross-facial nerve grafting, there is no distinct reason to avoid the single-stage

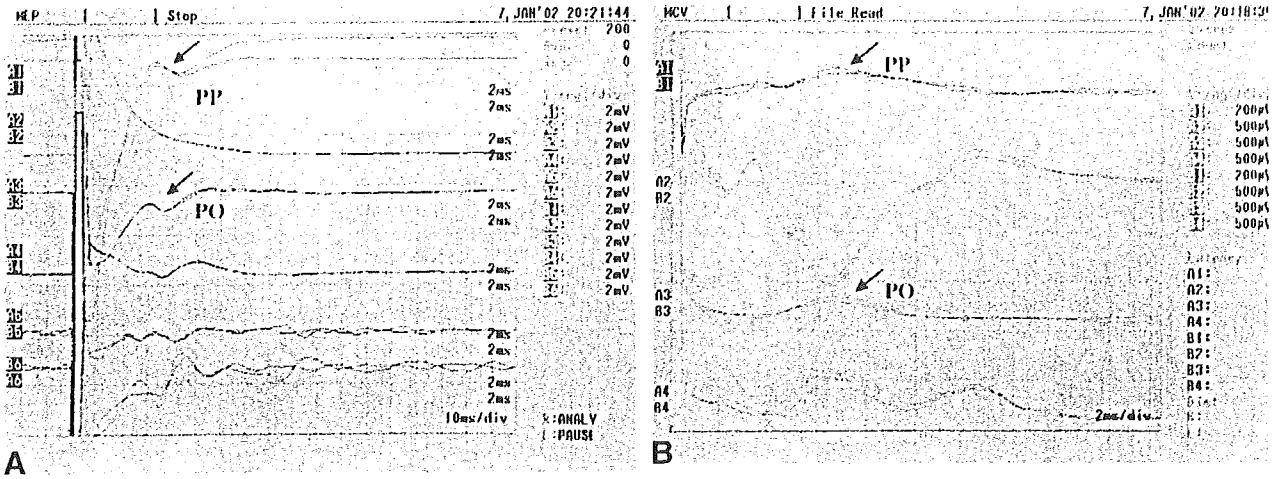


*Figure 4. Electroneuromyographic findings, 18 months after surgery. **A:** After stimulation of hypoglossal nerve on paralyzed side. Arrows indicate action potentials obtained from peripalpebral (PP) and perioral (PO) muscles on operated side. **B:** After stimulation of facial nerve on normal side. Arrows indicate action potentials obtained from peripalpebral (PP) and perioral (PO) muscles on operated side.*

Table 1. Recent Innovations in Reanimation Techniques for Reversible Facial Palsy*

Nerve crossover technique			
HGN-FN with interposition of nerve graft			
Side-to-end neurorrhaphy through partial neurectomy of HGN	May et al.	Otolaryngology	Reference 3
HGN-intratemporal FN			
Side-to-end neurorrhaphy through partial neurectomy of HGN	Sawamura and Abe	Neurosurgery	Reference 5
	Atlas and Lowinger	Otolaryngology	Reference 6
Side-to-end neurorrhaphy through epineural window of HGN	Koh et al.	Plastic surgery and neurosurgery	Reference 7
Combination of nerve crossover and cross-nerve grafting			
Two-stage procedure			
HGN-FN with division of branches, if necessary			
End-to-end neurorrhaphy	Endo et al.	Plastic surgery	Reference 11
Side-to-end neurorrhaphy through partial neurectomy of HGN	Mersa et al.	Plastic surgery	Reference 10
Side-to-end neurorrhaphy through perineural window of HGN and SNG-branches of paralyzed FN	Yoleri et al.	Plastic surgery	Reference 12
End-to-end neurorrhaphy			
Single-stage procedure			
HGN-intratemporal FN			
Side-to-end neurorrhaphy through partial neurectomy of HGN and SNG-trunk of paralyzed FN			
End-to-side neurorrhaphy through epineural window of FN	Present authors	Plastic surgery and neurosurgery	

**HGN, hypoglossal nerve; FN, facial nerve; SNG, sural nerve graft.*

procedure for early facial reanimation, especially in combination with the nerve crossover technique. Second, end-to-side neurorrhaphy was applied to create neural communications both between the distal stump of the facial trunk and the hypoglossal nerve, and between the end of the sural nerve graft and the main trunk of the paralyzed facial nerve. In the hypoglossal-facial nerve crossover, to prevent hemiglossal dysfunction, an anastomosis was performed on the partial neurectomy site of the hypoglossal nerve. In the cross-face nerve grafting, to preserve the whole continuity of the facial nerve plexus on the paralyzed side, an anastomosis was performed through the epineural window created by removal of the epineural sheath of the facial trunk. Regeneration of end-to-side nerve repair through the epineural window was proved by previous experimental and clinical studies.[7,14] The use of end-to-side neurorrhaphy in these studies not only decreased possible functional damage to the continuity of the hypoglossal and restored facial nerves, but also provided sufficient reinnervation of the facial nerve, based on clinical results and the findings of ENMG examinations.