Facial reanimation with interposition nerve graft or masseter nerve transfer: a comparative retrospective study

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Abstract

Both interposition nerve grafts and masseter nerve transfers have been successfully used for facial reanimation after irreversible injuries to the cranial portion of the facial nerve. However, no comparative study of these two procedures has yet been reported. In this two-site, twoarm, retrospective case review study, 32 patients were included. Of these, 17 patients (eight men and nine women, mean age 42.1 years) underwent interposition nerve graft after tumor extirpation or trauma between 2003 and 2006 in the Ear Institute, School of Medicine, Shanghai Jiao Tong University, China, and 15 patients (six men and nine women, mean age 40.6 years) underwent masseter-to-facial nerve transfer after tumor extirpation or trauma between November 2010 and February 2016 in Shanghai Ninth People's Hospital, China. More patients achieved House-Brackmann III recovery after masseter nerve repair than interposition nerve graft repair (15/15 vs. 12/17). The mean oral commissure excursion ratio was also higher in patients who underwent masseter nerve transfer than in patients subjected to an interposition nerve graft. These findings suggest that masseter nerve transfer results in strong oral commissure excursion, avoiding obvious synkinesis, while an interposition nerve graft provides better resting symmetry. This study was approved by the Institutional Ethics Committee, Shanghai Ninth People's Hospital, China (approval No. SH9H-2019-T332-1) on December 12, 2019. **Key Words:** facial palsy; facial reanimation; facial symmetry; House-Brackmann score; interposition; masseter nerve; nerve graft; oral commissure excursion; resting symmetry; synkinesis

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Introduction

Facial nerve paralysis has serious impacts on patients, including exposure keratopathy, impaired peripheral vision caused by brow ptosis, nasal obstruction because of loss of alar tone, dysarthria and impaired mastication caused by flaccidity of the cheek and lip, and oral incompetence. These conditions are not life-threatening, but can be extremely difficult for patients, both physically and mentally. Facial nerve paralysis is the most frustrating complication for both patients and surgeons after lateral cranial base surgery (Coulson et al., 2004). Although advances in skull base surgery have enabled neuro-otologists and neurosurgeons to spare the facial nerve in most cases, facial nerve resection remains necessary in

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1.5% to 2.5% of patients during tumor resection (Wilkinson et al., 2011; Ramos et al., 2015; Wang et al., 2015; Rozen et al., 2016).

There are several options after facial nerve sacrifice in tumor removal surgery. Immediate direct tension-free nerve coaptation is ideal, if possible; unfortunately, the surgical situation is frequently more complicated. When there is a substantial gap and the facial nerve ends cannot be coaptated without tension (even with rerouting), either interposition nerve grafting or cranial nerve transfer can be applied to reanimate the paralyzed face (Iseli et al., 2010).

Facial reanimation with the original proximal facial nerve end provides synchronized and spontaneous movement. Several studies have suggested that the long-term facial function of patients after intracranial facial nerve grafting is favorable, with 50% to 95% of patients achieving House-Brackmann (HB) grades III and IV (Iseli et al., 2010). In addition, it has been reported that hypoglossal nerve transfer can provide good clinical results, and this technique has been suggested as one of the standard procedures for facial reanimation (Hammerschlag, 1999; Yetiser and Karapinar, 2007). However, despite the advantages of these procedures, they have limitations that cannot be neglected, such as synkinesis or donor site morbidity, with impaired quality of life after reanimation. Over the last 10 years, masseter nerve transfer has been demonstrated to be a very reliable technique, and is favored by facial reanimation surgeons because of its high efficacy and minimal donor site morbidity (Wang et al., 2014). These reports are in line with our own observations, suggesting that selective coaptation of the masseter nerve maximizes clinical outcomes while reducing the extent of synkinesis.

However, the choice of facial reanimation after tumor removal depends largely on the personal experience or preferences of each surgeon, rather than clinical study-based evaluations. Comparative studies provide important information and can help clinicians in their day-to-day clinical practice. Several studies have compared the clinical outcomes of interposition nerve grafts with those of hypoglossal nerve transfer, and suggest that establishing immediate continuity of the facial nerve leads to superior results compared with alternatives such as facial-hypoglossal hookup; many such patients achieve HB grade III in the long-term, and benefit from avoiding a subsequent additional procedure (Malik et al., 2005; Wang et al., 2013). However, because of the site of injury in these cases, axon misdirection to the wrong target during regeneration is a major concern. Given the complexity of fiber function in the intracranial segment, massive synkinesis may be a major drawback. This can compromise a meaningful smile or facial expression, which is the key element for a real improvement in quality of life.

To the best of our knowledge, there are few comparative studies to date that compare the interposition nerve graft with masseter-to-facial nerve transfer. The aim of this study was to analyze the possible advantages and disadvantages of the two procedures through a retrospective review of two case series.

Subjects and Methods

Design

This was a two-site, two-arm study. Briefly, between 2003 and 2006, patients who underwent tumor extirpation or trauma and immediate repair by interposition nerve graft at the Ear Institute, Shanghai Jiao Tong University, School of Medicine (Shanghai, China; performed by the senior authors WH and WZY) were included in the interposition nerve graft group.

In the masseter nerve transfer group, patients were included who had undergone masseter-to-facial nerve transfer from 2010 to 2016 at Shanghai Ninth People's Hospital (Shanghai, China; performed by the senior author WW). The flow chart of patient inclusion is shown in **Additional Figure 1**. Patient selec-tion criteria were as follows: i) facial nerve injury occurred in the intracranial section in both groups; ii) normal preoperative facial nerve function (HB grade IV) (Croxson et al., 1990; Kanerva et al., 2011) or total tumor removal if facial palsy was caused by a tumor; and iii) immediate reanimation by interposition nerve graft after tumor extirpation or injury, or delayed repair by masseter nerve transfer within 2 years. The patients who were reanimated with masseter nerve transfer had a minimum 6-month delay after the facial nerve injury. This time period was required to avoid disturbing spontaneous recovery, if any, and to confirm complete facial palsy. A positive electromyography result of fibrillation potentials in the mimetic muscles of the affected side was also a prerequisite for the reconstructive procedure. In the interposition nerve graft group, all facial nerves were confirmed to be irreversibly damaged after tumor removal. A single surgeon (WW) performed all of the masseter-to-facial nerve transfer procedures, which involved the transfer of the descending branch of the masseter nerve to the distal buccal branch of the facial nerve, to innervate the paretic mimetic muscles. All patients began intensive biofeedback physical training in front of a mirror at 8 weeks postoperatively. A detailed description of these techniques was presented in a previous publication (Kanerva et al., 2011). Two different surgeons (WH and WZY) performed the interposition nerve graft repairs in patients who had facial nerve trauma or injury after tumor removal. Briefly, when a facial nerve defect was confirmed after trauma or tumor removal, a sural nerve graft was trimmed to the desired length to bridge the nerve defect. At the end of the surgery, closure was performed, involving four steps to avoid cerebrospinal fluid leakage when necessary: (1) suturing of the dura mater to minimize the opening; (2) occlusion of the antrum and the vestibulum with bone wax; (3) obturation of the surgical cavity with abdominal fat strips, and (4) middle ear exclusion in the case of a highly pneumatized temporal bone.

This study was approved by the Institutional Ethics Committee of Shanghai Ninth People's Hospital (approval No. SH9H-2019-T332-1) on December 12, 2019 (**Additional file 1**). Written informed consent was obtained from all patients, and the guidelines of the *Declaration of Helsinki* were followed throughout the study.

For all patients, their sex, age, and cause of disease at the time of surgery were documented. Demographic and medical variables were analyzed and correlated with their possible effects on the end results. Patient evaluations included physical examination, standard photographs and videos, facial symmetry score at rest (developed in our center) (Chen et al., 2017; **Table 1**), and facial function scoring using HB grades. Oral commissure excursion was measured quantitatively using FaceGram (Facial Nerve Center, Massachusetts Eye and Ear Infirmary, Boston, MA, USA). To limit bias caused by individual variances of the face, the distance of oral commissure excursion was converted to the ratio of oral commissure excursion in the affected side versus the contralateral unaffected side. Short-term (12 months) and long-term (\geq 36 months) follow-up data were collected from both groups.

Statistical analysis

Statistical comparisons were performed using parametric and non-parametric tests where appropriate, with SPSS software

Table 1 Clinical assessment scale for the oral commissure at rest			
Grade	Symmetry for the oral commissure		
4	Droop oral commissure with sagging skin		
3	Droop oral commissure without sagging skin		
2	Minimal asymmetry of oral commissure		
1	Symmetric oral commissure		

(IBM SPSS Statistics for Windows, Version 25.0, IBM Corp., Armonk, NY, USA). The chi-squared test was used for HB grade analysis, sex and cause of facial palsy analysis of the demographic data, and the independent *t*-test was used for age analysis, resting symmetry comparison, and FaceGram analysis. P < 0.05 was considered to indicate a statistically significant difference. Statements showing no difference between groups indicate that a statistical test was performed and failed to reject the null hypothesis.

Results

Demographic data of patients with interposition nerve graft or masseter-to-facial nerve transfer

The mean age of patients at the time of surgery was 40.6 years (24–70 years) in the masseter-to-facial nerve transfer group (n = 15) and 42.1 years (24–57 years) in the interposition nerve graft group (n = 17). There were no significant differences in age between the two groups (P > 0.05). The etiology of facial palsy included tumor extirpation and trauma that caused facial nerve injury from the cerebellopontine angle to the first bifurcation of the facial nerve. The denervation period before masseter nerve transfer ranged from 5 to 18 months, averaging 11.3 ± 3.7 months (**Table 2**). Mean follow-up times were 13.4 months (12–17 months) for the short-term study and 38.8 months (35–48 months) for the long-term study in the interposition nerve graft group, and 13.3 months (12–15 months) for the short-term study and 31.7 months (25–64 months) for the long-term study in the masseter nerve group.

Table 2 | Demographics of patients with interposition nerve grafts and masseter-to-facial nerve transfer

Characteristic	Interposition nerve graft	Masseter nerve transfer
Total patients (n)	17	15
Sex (male/female, n)	8/9	6/9
Age (yr, average (range))	42.1 (24–57)	40.6 (24–70)
Cause (n)		
Tumor resection	15	15
Trauma	2	-
Denervation time (mon, average (range))	0	11.3 (5–18)
Length of nerve graft (cm, average (range))	3.18 (2–5)	-

Data were analyzed using the chi-squared test (sex, cause) and independent-samples *t*-test (age).

Facial dynamic reanimation in patients with interposition nerve graft or masseter-to-facial nerve transfer

There was a significant improvement in facial nerve recovery (in terms of HB scores) in both groups compared with preoperative scores in the masseter group or immediately after surgery in the interposition group. The masseter nerve group had a significantly higher ratio of functional recovery compared with the interposition nerve graft group (P < 0.05). In the interposition nerve graft group, HB grade III facial function was achieved in six (35%) and 12 (71%) of the 17 patients in the short- and long-term follow-up periods, respectively, compared with 0 immediately after the procedure (P < 0.05). There was also a significant difference in facial recovery results between the short- and long-term follow-up periods in the interposition nerve graft group (P < 0.05). In the masseter nerve transfer group, HB grade III facial function was achieved in all 15 patients in the short-term time period, compared with 0 pre-operation (P < 0.05); this result remained unchanged in the long-term follow-up (**Table 3**).

Table 3 $\,\mid\,$ House-Brackmann scores of patients with interposition nerve grafts and masseter-to-facial nerve transfer

	Short term	Long term
Interposition nerve graft group		
Grade III (n)	6	12*
Grade IV (n)	11	5
Masseter nerve transfer group#		
Grade III (n)	15	15
Grade IV (n)	0	0

Data were analyzed using the chi-squared test. *P < 0.05, vs. short term; #P < 0.05, vs. interposition nerve graft group. Short term: 12 months; long term: \ge 36 months.

The oral commissure excursion improved in both groups. The mean ratio of oral commissure excursion versus the contralateral unaffected side was 97% in the reanimated side of the masseter nerve group, which was similar to the contralateral healthy side. This ratio was significantly higher than that of the affected side of the interposition nerve graft group (82%, P < 0.01) in the long-term follow-up. The oral commissure excursion in the reanimated side of the interposition nerve graft group was significantly lower than that of the contralateral unaffected side in all cases (P < 0.01). A relatively strong smile was observed in most patients in the interposition nerve graft group, although smiles remained asymmetrical (**Figure 1**).

Using our facial symmetry score at rest, the mean score for patients reanimated with interposition nerve graft was 1.6 ± 0.7 at the long-term follow-up, compared with $2.3 \pm$ 1.1 after masseter nerve transfer. These values were not significantly different (*P* > 0.05), although the masseter nerve results appeared higher than the results of the reanimated side of the interposition nerve graft. However, slight or obvious asymmetry in the lower lip was noted in both groups (**Figure 1**).

Slight or no synkinesis was observed in the patients reanimated by masseter nerve transfer. Moreover, synkinetic contracture was confined to the orbicularis oculi only. This was not reported as disturbing by the patients, because the orbicularis oculi naturally contracts in a smile, so the patients were able to deliver pleasant and meaningful smiles (**Figure 1**). However, in the interposition nerve graft group, severe hemiface synkinesis was observed in some of the patients with relatively strong to moderate smiles. Synkinetic frowning, eye closure, oral commissure depression, and mentalis contraction were activated simultaneously while smiling, resulting in awkward and confusing expressions (Figures 1 and 2). This became even more obvious when a mirrored full face was generated from each hemiface (Figure 2). In patients with no or slight synkinesis, facial movements (including the oral commissure excursion in the affected side) were also generally weak, and patients displayed a frozen face (Figure 3). Spontaneous smiles developed in all patients in the interposition nerve graft groups, but in no patients in the masseter-to-facial nerve transfer group.



Figure 1 | Facial expressions after reanimation with masseter nerve transfer or interposition nerve graft. (A) A 28-year-old woman at 36 months after masseter nerve transfer. (B) A 41-year-old man at 36 months after interposition nerve graft.



Figure 2 | Mirrored smile by FaceGram.

A 41-year-old man at 36 months after interposition nerve graft repair. Left: original smile; middle: mirrored smile generated from the unaffected (right) side; right: mirrored smile generated from the affected (left) side. Arrows: synkinetic movements (frowning, eye closure, depression of the oral commissure, and mentalis contraction). Arrowhead: compensatory eyebrow lifting in the unaffected side.



Figure 3 $\ \mid$ Patients with no evident synkinesis also displayed weak muscle function.

A 44-year-old man at 3 years after interposition nerve graft repair. From left to right: At rest, eye closure, puckering, smiling.

Discussion

The incidence of facial nerve interruption has been markedly reduced by improvements in surgical techniques and perioperative monitoring. It has been reported that facial nerve preservation is achieved in > 90% of large vestibular schwannoma patients. However, a certain degree of facial interruption is inevitable, particularly in patients with large or recurrent tumors (Hertzano and Eisenman, 2011). Various techniques can be used for facial reanimation, depending on the characteristic of the proximal stump of the facial nerve and the surgeon's preference (Guntinas-Lichius et al., 2007). Direct nerve repair has always been the first choice after facial nerve injury, in the central part if possible. There is also evidence that direct nerve coaptation can achieve the best results (Eaton et al., 2007). However, if a nerve defect cannot be repaired by direct neurorrhaphy, it has been suggested that an interposition nerve graft is superior to a hypoglossal nerve transfer (Malik et al., 2005; Wang et al., 2013). With the advent of the masseter nerve transfer, it is worthwhile to compare these two techniques, because the masseter nerve transfer is a highly efficient and reliable new technique for reanimating the paralyzed face.

The masseter nerve transfer has become a favored procedure by many facial reanimation surgeons over the last 10 years. This technique is favored because of its advantages of a close vicinity to the recipient facial nerve, large axonal load, strong muscle contraction, and minimal donor site morbidity (Coombs et al., 2009). In most cases, strong muscle contraction can be observed by 6 months after this procedure. Furthermore, 100% of the patients in the present study showed recovery, with HB score III facial function, despite the minimum 6-month delay compared with the interposition nerve graft group. This result remained stable over the 3-year follow-up period. The only shortcoming of this procedure is that the innervation comes not from the original facial nucleus, but from the motor nucleus of the trigeminal nerve. Good control of smile therefore requires postoperative rehabilitative training, and spontaneous smiles are less likely, although several papers have reported spontaneous smiles after this procedure. There is some evidence that 40% of the population have simultaneous excitation of the masseter muscle during smiling, which suggests that spontaneous smiles might be possible with proper training (Schaverien et al., 2011; Hontanilla and Marre, 2014).

Interposition nerve graft with the sural nerve, in contrast to masseter nerve transfer, has the advantage of yielding emotion-driven, spontaneous smiles after the procedure without the need for rehabilitative training, because the nerve supply is from the original facial nucleus. Facial function recovery with this procedure generally produces good results, with the best outcome of HB grade III facial function (Humphrey and Kriet, 2008). In line with previous literature, we also observed recovery of facial function, with HB grade III in six and 12 of the 17 patients at the short- and long-term follow-ups, respectively.

However, asymmetry during smiling remained obvious in most patients in the interposition nerve graft group. Muscle contraction and oral commissure excursion in this group was not as strong as in the contralateral healthy side or compared with the masseter nerve group. Studies by Humphrey and Kriet (2008) suggested that functional outcomes after facial reanimation depend greatly on the axonal load in the donor nerve. In the interposition nerve graft group, the regenerating nerve needed to pass two coaptations, and scar tissue may have impeded nerve growth through the anastomoses. The distance of nerve regeneration was also longer in this group, leading to longer denervation times for the mimetic muscles. Furthermore, because the injury was closer to the nucleus of the facial nerve, more severe damage was induced to the facial nucleus neurons compared with the masseter nerve transfer group, in which the injury site was close to the terminal part of the masseter nerve. In addition, with masseter nerve transfer, the descending branch of the masseter nerve was physically coaptated to the buccal branch of the facial nerve, ensuring regeneration of most nerve fibers into the upper lip muscles. In contrast, in the interposition nerve graft group, neurorrhaphy was performed between the nerve graft and the main trunk of the facial nerve. Because of the lack of selective regeneration, there can be large variances in the actual percentages of nerve fibers that originally innervated, and will again accurately innervate, the same target muscle (Al-Majed et al., 2000; Aikeremujiang et al., 2015; Wood and Mackinnon, 2015).

The most common complication of interposition nerve graft repair is synkinesis. Following surgery, synkinesis developed in most of the interposition nerve graft cases in the present study, and included frowning, eye closure, and depression of the oral commissure and muscle bundles in the neck. Minor synkinesis was also observed in the masseter nerve transfer group, confined to the periocular region. Despite spontaneous responses to humorous stimuli, insufficient and awkward smiles were generated, delivering confusing information. The ultimate goal of facial reanimation is to reconstruct an emotionally controlled, meaningful smile and facial expressions; this is considered the key element for actual improvements in quality of life. To this end, a good understanding of facial muscle function is necessary. A meaningful smile not only involves activation of the levator muscles, but also a delicate balance with the depressor muscles and coordination with the periocular muscles. Synkinesis, or disorders in facial muscle function, can result in unnatural expressions, which provide confusing information and impair social interactions. With 22 pairs of mimetic muscles, the facial nerve encompasses numerous nerve bundles that are arranged in different patterns along the pathway from the brainstem to target muscles, forming an extremely complex network. If there is a lack of selective regeneration, the regenerating nerves project randomly into the distal nerve stumps and extend collaterals to increase the chance of finding the proper target organs; this greatly increases the chances of synkinesis in later stages (Franz et al., 2005; Wang et al., 2009). Furthermore, it has been reported that accurate coaptation with an epineural suture does not decrease the chance of misprojection. Synkinesis after an interposition nerve graft is inevitable, and the confusing and unpleasant facial expressions that occur after nerve regeneration can make life difficult for patients. To achieve a meaningful and natural smile, we developed the idea of subunit-based reconstruction, in which the upper lip, lower lip, and periocular region should be treated as separate subunits, if it is believed that the reanimation will result in severe synkinesis. With masseter nerve transfer, surgeons should be allowed to choose proper distal recipient nerves. Instead of coaptating the masseter nerve to the main truck, as in the early years of this technique, the descending branch of the masseter nerve can be selectively coaptated to the upper buccal branch, which mainly controls the levator muscles of the upper lip, with minimal innervation to the orbicularis oculi muscle. Thus, severe synkinesis of eye closure can be minimized.

Innervation by neurons from the facial nucleus is more likely to result in good muscle tone, which maintains good resting symmetry. Our recent study (unpublished data) suggested that masseter nerve transfer in cases with preoperative drooping of the oral commissure has limited, if any, contribution to mimetic muscle tone and resting symmetry. Nevertheless, we recommend caution when making any conclusions based on the current study, because all of our interposition nerve grafts were performed immediately after tumor extirpation. In addition, limited graphic data are available from previous publications of interposition nerve graft studies. It is also worth noting that interposition nerve grafts achieve better results in sphincters, with better eye closure, oral competence, and buccinator function, which might further contribute to resting symmetry and may be important for functional improvements of dry eyes, food retainment, and oral competence. These improvements are difficult to achieve with masseter nerve transfer. Therefore, it may be possible to combine these two procedures together in the future, either by end-to-end or end-to-side coaptation, to reconstruct a strong and natural smile by masseter nerve activation, without

triggering synkinesis by the facial nerve. At the same time, eye closure, oral competence, and buccinator function can be improved with interposition nerve grafts. Results supporting this concept have been reported recently; a combination of multiple nerve sources provided better results (Biglioli et al., 2018a, b). This could be because of the mutual promoting effect of regeneration (Gesslbauer et al., 2017). However, the efficacy of end-to-side coaptation has long been controversial. Studies have also suggested that opening a window in the perineurium may increase the efficacy of nerve regeneration (Papalia et al., 2016; Geuna et al., 2017).

One limitation of the present study is that the two groups of patients were not consistent with regard to pre-operative facial function. Patients in the interposition nerve graft group had normal facial function before the reanimation surgery, whereas most patients from the masseter-tofacial nerve transfer group had at least a 6-month delay before the reanimation procedure. This was not an issue for the comparison of oral commissure excursion, because the masseter-to-facial nerve transfer resulted in a better functional outcome, despite worse preoperative function. In contrast, it may have interfered with the analysis of postoperative resting symmetry. Furthermore, the patients in the two groups were from two different centers and the two procedures were performed by different surgeons, although the sites of nerve injury were all located in the intracranial section. All interposition nerve graft cases were operated on by the second- and third-to-last senior authors (WH and WZY), while the masseter nerve surgeries were all performed by the senior author (WW). However, each of the senior authors is proficient in their area of expertise. In addition, the patients included in this retrospective study were not operated on during exactly the same period of time. In all of the interposition nerve graft cases, the nerve repair was performed immediately after the tumor extirpation, while there was at least a 6-month delay before nerve repair in the masseter nerve transfer group. These factors might bias the final results, and a prospective study is needed to confirm our results.

In this retrospective study, we successfully compared the interposition nerve graft with the masseter nerve transfer. We revealed that the masseter nerve transfer is a valuable alternative to interposition nerve grafts after skull base tumor extirpation and subsequent nerve defects, and leads to a strong, symmetrical, and natural smile. In contrast, the interposition nerve graft provides good resting symmetry and better improvements in eye closure, oral competence, and buccinator function. A combination of these two procedures might be possible in the future to generate optimal outcomes.

Author contributions: Surgical procedures: ZYW, HW, WW; data analysis: WJW, WDZ, GC; manuscript drafting: WJW; manuscript revision: WDZ, MT, ZYW, HW, WW. All authors approved the final version of the paper. Conflicts of interest: There were no conflicts of interest in this experiment.

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clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity.

Reporting statement: This study follows the Transparent Reporting of Evaluations with Nonrandomized Designs (TREND) guidance for protocol reporting.

Biostatistics statement: The statistical methods of this study were reviewed by the biostatistician of School of Public Health, Fudan University.

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Open peer reviewers: Michele R Colonna, Universita degli Studi di Messina, Italy; Erol Benlier, Trakya University, Turkey. **Additional files:**

Additional file 1: Hospital Ethics Approval (Chinese).

Additional file 2: Open peer review report 1.

Additional Figure 1: Flow chart for case inclusion and exclusion in interposition nerve graft (A) and masseter to facial nerve transfer (B) groups.

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Excluded

Additional Figure 1 Flow chart for case inclusion and exclusion in interposition nerve graft (A) and masseter to facial nerve transfer (B) groups. EMG: Electromyography; HB: House-Brackmann.