The Degree of Facial Movement following Microvascular Muscle Transfer in Pediatric Facial Reanimation Depends on Donor Motor Nerve Axonal Density

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THERAPEUTIC

Background: Free functional muscle transfer to the face is a standard of facial animation. The contralateral facial nerve, via a cross-face nerve graft, provides spontaneous innervation for the transferred muscle, but is not universally available and has additional shortcomings. The motor nerve to the masseter provides an alternative innervation source. In this study, the authors compared donor nerve histomorphometry and clinical outcomes in a single patient population undergoing free muscle transfer to the face.

Methods: Pediatric patients undergoing dynamic facial (re-)animation with intraoperative nerve biopsies and gracilis transfer to the face powered by either the contralateral facial nerve via a cross-face nerve graft or the motor nerve to the masseter were reviewed over a 7-year period. Myelinated nerve counts were assessed histomorphometrically, and functional outcomes were evaluated with the Scaled Measurement of Improvement in Lip Excursion software.

Results: From 2004 to 2011, 91 facial (re-)animation procedures satisfied study inclusion criteria. Average myelinated fiber counts were 6757 per mm2 in the donor facial nerve branch, 1647 per mm^2 in the downstream cross-face nerve graft at the second stage, and 5289 per mm^2 in the masseteric nerve. Reconstructions with either innervation source resulted in improvements in oral commissure excursion and smile symmetry, with the greatest amounts of oral commissure excursion noted in the masseteric nerve group.

Conclusions: Facial (re-)animation procedures with use of the cross-face nerve graft or masseteric nerve are effective and result in symmetric smiles. The masseteric nerve provides a more robust innervation source and results in greater commissure excursion. (*Plast. Reconstr. Surg.* 135: 370e, 2015.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, III.

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Facial paralysis is devastating. Patients may endure functional consequences of facial palsy, including corneal irritation, external nasal valve collapse, speech difficulties, and oral incompetence, but often experience an even greater psychosocial burden. The treatment of facial paralysis was revolutionized by the description of free functional muscle transfer to the face in the 1970s.[1] In the original description by Harii et al., the deep temporal nerve was used to power the free gracilis muscle. Since then, many innervation sources have been used to power the transferred muscle.[2–11] In cases of unilateral facial paralysis, the contralateral, normal facial nerve is a common donor and has long been considered the criterion standard donor nerve source. Despite its spontaneity and success, the contralateral facial nerve is not always available, requires a nerve graft, typically entails two surgical procedures, and often offers modest improvements in movement of the affected oral commissure, leaving room for improvement and a role for alternative donor nerve sources.

The motor nerve to the masseter muscle (masseteric nerve) addresses some of the contralateral facial nerve's shortcomings. In a single-stage technique, the masseteric nerve permits direct nerve transfer without the need for a graft and generates greater commissure excursion compared with muscles innervated by cross-face nerve grafts.[12–14] In a comparison study of patients who had dynamic facial reconstruction powered by either the contralateral facial nerve and cross-face nerve graft or the masseteric nerve, our group has previously described increased amounts of oral commissure excursion in the masseteric nerve group, with oral commissure excursion in this group nearly identical to the unaffected side.[13] Previous nerve studies have demonstrated increased axonal counts in the masseteric nerve for nerve grafting procedures compared with the facial nerve and cross-face nerve grafting.[15,16] We hypothesize that increased commissure excursion results from a more robust axonal supply in the innervation source. To our knowledge, no prior studies have correlated nerve histomorphometry from different innervation sources to functional outcomes in patients undergoing free functional muscle transfer to the face. In this study, we demonstrate increased oral commissure excursion in patients undergoing dynamic reconstruction using the masseteric nerve and greater axonal numbers in the masseteric nerve compared with the cross-face nerve graft at the time of microvascular gracilis muscle transfer.

PATIENTS AND METHODS

We evaluated our experience with dynamic facial animation procedures for children with complete facial paralysis from 2004 to 2011 at The Hospital for Sick Children. The research protocol was approved by the Research Ethics Board of The Hospital for Sick Children. Patients were included in the study that had undergone intraoperative nerve biopsy and reconstruction by means of one of two techniques. In the first technique, patients underwent a two-stage reconstruction using the contralateral normal facial nerve by means of a cross-face nerve graft followed by coaptation of the downstream cross-face nerve graft to the gracilis motor branch of the obturator nerve at the time of microvascular segmental gracilis muscle transfer. In the second technique, patients underwent a single-stage reconstruction during which the ipsilateral masseteric nerve was transferred to the gracilis motor nerve at the time of microvascular gracilis muscle transfer. For the two-stage technique, intraoperative nerve biopsies were performed for the donor contralateral facial nerve branch at the time of the first procedure and the downstream cross-face nerve graft and the gracilis motor branch of the obturator nerve at the second operative procedure. Similarly, the masseteric nerve and the gracilis motor branch of the obturator nerve were submitted to biopsy during the single-stage technique. [**See Figure, Supplemental Digital Content 1**, which illustrates intraoperative neural biopsy sites, ***http://links.lww.com/PRS/B198***. Regions of intraoperative nerve biopsy are illustrated with red arrows for the two-stage technique (*above*) and the single-stage technique (*below*). *VII*, contralateral facial nerve donor branch; *CFNG*, cross-face nerve graft at the time of the second operative stage; *Obturator nerve*, motor nerve branch to gracilis from obturator nerve; *Masseteric nerve*, motor nerve branch to masseter.]

Histomorphometry

Tissue samples were fixed in glutaraldehyde. Samples were embedded in epoxy resin and then stained with toluidine blue to allow direct histomorphometric analysis with optimal clarity and detail. Myelinated axons were counted from a representative area of nerve with the aid of Image Tool (University of Texas Health Sciences Center, San Antonio, Texas) to produce counts per square millimeter. A single individual performed all nerve processing and staining procedures; counting was also uniformly performed by a single individual.

Patients without complete histomorphometry counts for all operations were excluded.

Clinical Evaluation

Clinical outcomes were assessed with the Scaled Measurement of Improvement in Lip Excursion software,[17] a validated instrument that uses iris diameter, which is conserved in humans, as a scale of reference for all facial features within a photograph. Frontal photographs of patients at resting facial expression and at maximal smile were analyzed preoperatively and postoperatively. The assessed measurements are depicted. [**See Figure, Supplemental Digital Content 2**, which shows facial measurements performed with Scaled Measurement of Improvement in Lip Excursion (*SMILE*) software, ***http://links.lww.com/PRS/B199***. The oral commissure position measurements are illustrated on the photographs for commissure excursion improvement (*green hypotenuse, above*), excursion asymmetry (*bilateral green hypotenuses, center*), and vertical height asymmetry (*bilateral blue lines, below*). The formulas used to calculate each of these values accompany each photograph.] Oral measurements used a right-angle triangle drawn from the midline lower lip vermilion-cutaneous junction. A single individual repeated measurements in triplicate for all patients. Improvement in oral commissure excursion, calculated as the postoperative hypotenuse (smile-rest) minus the preoperative hypotenuse (smile-rest); asymmetry in oral commissure excursion, calculated as the contralateral hypotenuse (smile-rest) minus the ipsilateral hypotenuse (smile-rest positions); and asymmetry in vertical position of the oral commissure, calculated as the contralateral commissure height minus the ipsilateral commissure height, were determined for all patients. Patients without complete preoperative and postoperative photographic sets were excluded.

Statistical Analysis

Data were tested with the *t* test using Excel (Microsoft Corp., Redmond, Wash.) spreadsheets and formulas. Statistical significance was defined as $p < 0.05$.

RESULTS

Study Population

During the study period, 91 dynamic facial animation procedures were performed with intraoperative nerve biopsy using either the contralateral facial nerve or the ipsilateral masseteric nerve as donors. Complete histomorphometric data were available for 68 procedures. The masseteric nerve was used to power the transferred gracilis muscle in 23 single-stage procedures. The contralateral facial nerve and cross-face nerve graft (two-stage technique) were used to power the transferred gracilis muscle in 45 procedures. Of the 45 two-stage procedures, complete information was available for both operative stages for 17 patients (34 procedures). Complete sets of preoperative and postoperative photographic data were available for 13 single-stage (masseteric nerve) reconstructions and for 12 patients who completed the two-stage (contralateral facial nerve and cross-face nerve graft) reconstruction. (**See Figure, Supplemental Digital Content 3**, which shows the study population, ***http://links.lww.com/PRS/B200***. Ninety-one facial animation procedures with intraoperative nerve biopsy and reconstruction with either the two-stage technique with cross-face nerve graft or the single-stage technique with the masseteric nerve were performed during the study period. *CFNG*, cross-face nerve graft; *FP*, facial palsy. Details of the patient population included in the study are illustrated.)

There were no relevant differences in demographics between the groups undergoing reconstruction with the two techniques (Table 1). The average age at the time of reconstruction was 10.2 years in the two-stage group (facial nerve and cross-face nerve graft) (average between two stages) and 9.6 years in the single-stage group (masseteric nerve) ($p < 0.68$). For the two-stage cross-face nerve graft group, an average interval of 381 ± 235 days passed between the two stages. The average length of the cross-face nerve graft was 13.6 ± 2.2 cm. The average weight of the transferred segment of gracilis muscle was 17.9 g in the two-stage technique and 14.1 g in the single-stage technique ($p < 0.03$). All patients undergoing reconstruction with the masseteric nerve had a congenital facial paralysis, and half of the patients undergoing reconstruction with the contralateral facial nerve and cross-face nerve graft had a congenital facial palsy ($p < 0.00001$).

Myelinated Axonal Counts

Average myelinated fiber counts are summarized in Figure 1. For the two-stage technique, the donor branch of the contralateral facial nerve

Table 1. Patient Demographics

	CFNG	Masseteric	*p*
Age at surgery, mo	122	115	<0.68
Segmental gracilis weight, g	17.9	14.1	<0.026
Congenital cause, %	0.5	1.0	<0.00001

CFNG, cross-face nerve graft.

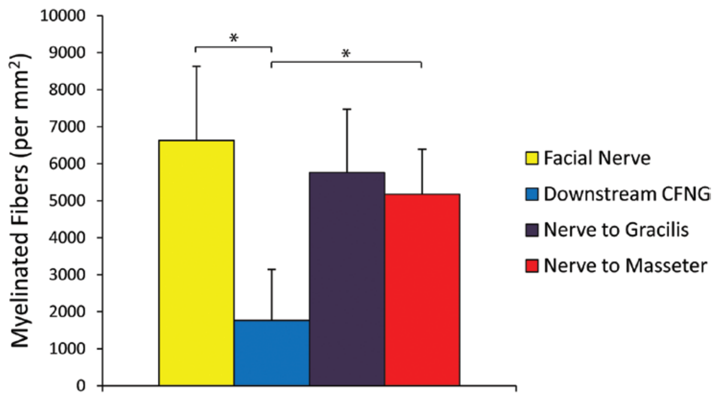

Fig. 1. Average myelinated axon counts from donor and recipient nerves. Histomorphometric analyses were performed after intraoperative nerve biopsy, and average myelinated axon densities are displayed for each nerve source. *Error bars* = SD.

exhibited an average of 6757 myelinated fibers per square millimeter. At the time of the second operative procedure, the downstream cross-face nerve graft had an average of 1647 axons per square millimeter, a 76 percent decrease in myelinated fibers from the donor facial nerve. For the single-stage technique, the masseteric nerve demonstrated an average of 5289 myelinated fibers per square millimeter. For all groups, the gracilis motor branch of the obturator nerve averaged 5808 myelinated axons per square millimeter.

Clinical Outcomes

Graphic depictions of Scaled Measurement of Improvement in Lip Excursion measurements are illustrated in Figure 2. There were no muscle failures. Improvements in oral commissure excursion were noted postoperatively in patients undergoing reconstruction with either technique. Significantly greater gains in commissure excursion on the affected side of the face were noted in patients undergoing reconstruction with the masseteric nerve (8.1 ± 4.0 mm) compared with the two-stage technique using the facial nerve and cross-face nerve graft (4.1 ± 2.9 mm; $p < 0.026$) (Fig. 2, *above, left*). There were no differences in postoperative commissure excursion of the unaffected side of the face between the two techniques ($p < 0.93$), indicating that use of a donor branch from the facial nerve does not produce a deficit. Although absolute commissure excursion is an important outcome measure, symmetry should not be overlooked in smile analysis. The two-stage cross-face nerve graft group demonstrated larger amounts of preoperative commissure excursion asymmetry. Postoperatively, both innervation sources provided relatively symmetric oral commissure excursion. Patients undergoing reconstruction with the two-stage technique gained an average of 6.5 mm of improvement in excursion symmetry ($p < 0.001$). The single-stage masseteric nerve group had no significant changes in oral commissure excursion asymmetry ($p < 0.41$), with minimal asymmetry postoperatively (Fig. 2, *above, right*). Asymmetries in the vertical position of the oral commissures were also assessed. Both groups of patients demonstrated asymmetries in vertical height of the commissures preoperatively, particularly when smiling. Reconstructions with both innervation sources resulted in significant improvements in symmetry of the commissure vertical height in the smiling position, by 6.2 mm in the two-stage cross-face nerve graft group ($p < 0.0001$) and by 9.9 mm in the single-stage masseteric nerve group ($p < 0.021$) for patients affected with unilateral facial paralysis (Fig. 2, *below*). There were no differences between preoperative and postoperative vertical height asymmetries for patients affected with bilateral facial paralysis ($p < 0.69$, smile position; $p < 0.46$, rest position).

Representative preoperative and postoperative photographs are shown for patients undergoing smile reconstruction with the two-stage cross-face nerve graft technique (Figs. 3 and 4) and the single-stage technique with the masseteric nerve (Figs. 5 and 6).

DISCUSSION

Both the contralateral facial nerve and the ipsilateral masseteric nerve provide excellent nerve sources to power free gracilis transfers for facial animation. Both donor nerves produced improvements in oral commissure excursion and elevation in our pediatric population. Each

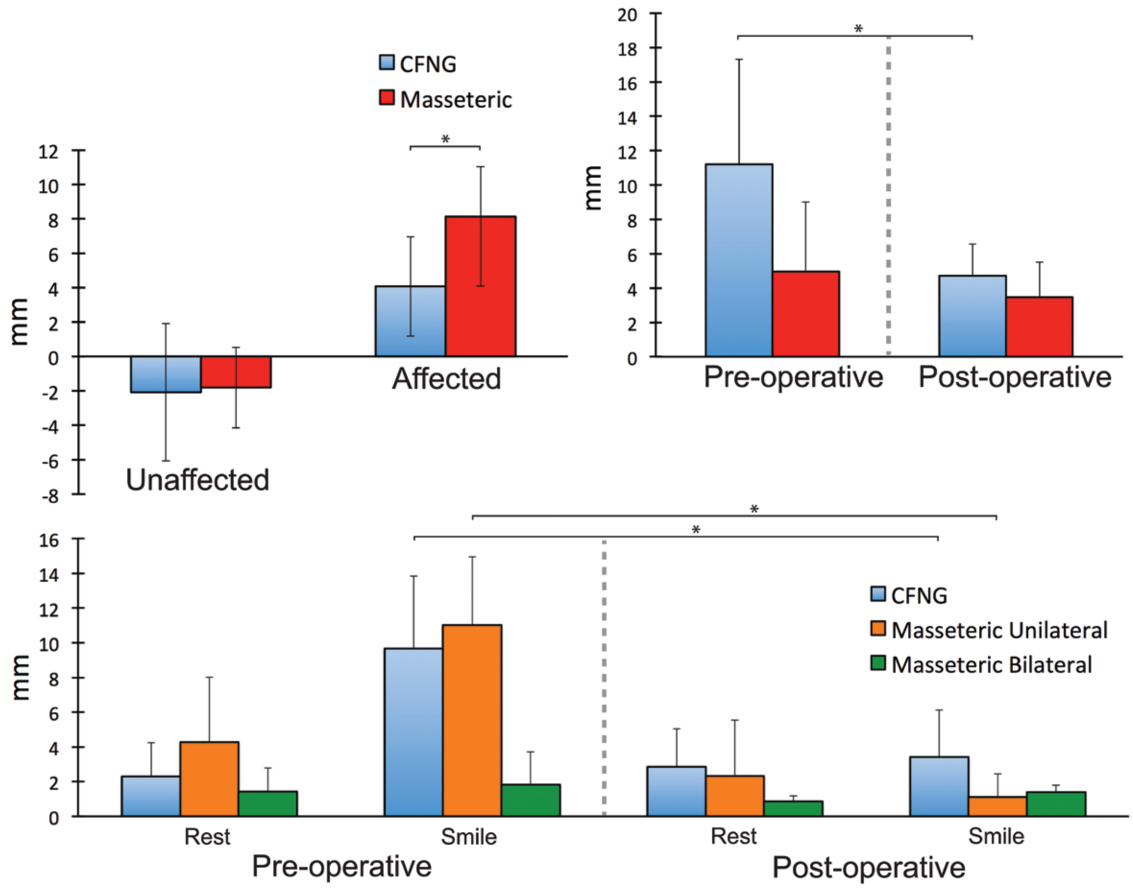

Fig. 2. Graphic summaries of Scaled Measurement of Improvement in Lip Excursion measurements. Average facial measurements for patients undergoing smile reconstruction with either the two-stage technique with the contralateral facial nerve and cross-face nerve graft (*CFNG*) or the single-stage technique with the motor nerve branch to the masseter nerve are summarized for improvement in oral commissure excursion (*above*, *left*), improvement in commissure excursion asymmetry (*above*, *right*), or improvement in commissure vertical height asymmetry (*below*). The *vertical axes* represent distance in millimeters. Comparisons are made between the nonparalyzed (unaffected) and paralyzed (affected) sides of the face (*above*, *left*) and preoperative and postoperative values (*above, right and below*). Patients treated with the single-stage masseteric nerve technique are divided into patients with unilateral (masseteric unilateral) and bilateral (masseteric bilateral) facial paralysis in the lower graph. *Error bars* = SD.

of these donor nerves has specific advantages and disadvantages. Each technique may be preferred in certain circumstances, such as bilateral facial paralysis, potential need for future Le Fort I orthognathic procedures, unwillingness to undergo staged surgical procedures, failed previous cross-face nerve graft, desire to avoid motor reeducation postoperatively, desire for emotional smile, or other patient or family preferences.

Of the two nerve sources available to power the free functional muscle transfer, we observed a more than 3-fold greater number of axons in the masseteric nerve compared with the downstream cross-face nerve graft. The masseteric nerve source does not require a nerve graft and has one less coaptation site, which both decrease axonal dropoff. Similar to our results in which we observed only 24 percent of the donor facial nerve axons arriving in the downstream cross-face nerve graft, other groups have noted only 20 to 50 percent of axons crossing a nerve graft.[18–20] The functional significance of these quantitative differences in axonal supply may be considerable. Animal studies have shown that force deficits in transplanted muscle correlate with decreased axonal supply,[21] a minimum requirement of only 12 percent of normal axon load to reinnervate mimetic musculature,[22] and maintenance of 30 percent of innervation to sustain skeletal muscle force generation.[23] The idea that axonal supply affects facial movement has been postulated,[19,24–27] and Urso-Baiarda et al.[28] suggest dynamic facial reconstruction to be limited ideally by muscle factors rather than by axonal supply to reestablish normal physiology. In this

Fig. 3. Patient with left unilateral facial paralysis undergoing smile reconstruction with free functional gracilis transfer to the face with the two-stage technique using the contralateral facial nerve and cross-face nerve graft . Preoperative photographs at rest (*above*, *left*) and smiling (*above*, *right*) show asymmetries in oral commissure vertical height and excursion. Postoperative photographs at rest (*below*, *left*) and while smiling (*below*, *right*) illustrate improvements in commissure excursion and symmetry.

"muscle bottle-necked system," muscle fibers are fully reinnervated, producing normal motor unit size, resulting in optimal muscle force that is resistant to small fluctuations in axon number. In contrast, "nerve bottle-necked muscle," which results from small axonal input, creates enlarged motor units that may have a variable functional response to small differences in axonal supply. Terzis et al.[27] suggested a minimum axonal count of 900 for donor facial nerve branches to yield satisfactory clinical results. Facial movements, however, have not previously been measured quantitatively in conjunction with histomorphometry in the same patient population.

Fig. 4. Patient with right unilateral facial paralysis undergoing smile reconstruction with free functional gracilis transfer to the face with the two-stage technique using the contralateral facial nerve and cross-face nerve graft. Preoperative photographs demonstrate minimal commissure asymmetry at rest (*above*, *left*), but asymmetries in commissure excursion and vertical position are obvious with animation (*above*, *right*). Postoperatively, the patient has maintained oral symmetry at rest (*below*, *left*) and significant improvements in smile symmetry with new right commissure excursion in a natural oblique vector (*below*, *right*).

Our myelinated axon densities are greater than most described. Donor facial nerve branches have been described to contain 683 to 1736 myelinated fibers and distal cross-face nerve graft to contain 100 to 453 myelinated fibers, with large standard deviations.[19,20,27] Similarly, the numbers of myelinated axons in the masseteric nerve have previously been described as 1543 to 2775 with variance,[15,16] significantly less than our average count of 5289. These differences may result from our counting technique, with the use of Image Tool, which was not used

Fig. 5. Patient with bilateral facial paralysis undergoing smile reconstruction with free functional gracilis transfer to the face with the single-stage technique using the masseteric nerve. Preoperative photographs at rest (*above*, *left*) and while smiling (*above*, *right*) show little difference in facial expression except for left lower lip depression with attempted animation. Postoperative photographs at rest (*below*, *left*) and while smiling (*below*, *right*) demonstrate oral commissure symmetry with improved excursion and minimal facial bulk.

in previous studies. We describe myelinated axon counts in fibers per square millimeter, as this has been the technique used at our institution for many years. Given that a single individual performed all histomorphometric analyses, the data describe our institution's experience over time. Our data trends are true and provide an important message about relative fiber counts, even if our absolute numbers differ from those elsewhere.

Although reports of use of the masseteric nerve as a donor for facial movement date to the 1970s,[29] use of this donor has been relatively rare. Unfamiliarity with its anatomical location, donor

Fig. 6. Patient with bilateral facial paralysis undergoing smile reconstruction with free functional gracilis transfer to the face with the single-stage technique using the masseteric nerve. Preoperative photographs at rest (*above*, *left*) and while smiling (*above*, *right*) show absence of facial movement and incompetence to oral secretions. Postoperative photographs at rest (*below*, *left*) and while smiling (*below*, *right*) demonstrate lower lip support and a symmetric smile.

deficit concerns, motor reeducation concerns, and lack of spontaneous smile have limited its use. The masseteric nerve has multiple branches, allowing its use without donor-site morbidity.[30,31] The reliability of its anatomical location has been well described.[16,32–34] Manktelow et al.[35] describe that of 27 adult patients who underwent free gracilis transfer to the face neurotized with the masseteric nerve, 89 percent reported a spontaneous smile some of the time, and 85 percent of patients were able to smile without biting. Similarly, Lifchez et al.[36] noted spontaneous smiles in seven patients with Möbius syndrome who had undergone facial animation with muscle transfer and neurotization with the masseteric nerve. In their native function, the masseteric nerve and facial nerve differ in strength and scale of movement. To address concerns of less specific and intuitive reconstructed movement with use of the masseteric nerve, double innervation of free muscle transfers with both the masseteric nerve and the facial nerve by means of a cross-face nerve graft has been suggested to optimize strength and spontaneity of movement.[11]

In our study, both nerve sources contributed to improved oral commissure excursion and smile symmetry, but use of the masseteric nerve resulted in greater oral commissure excursion. Normal commissure excursion in people not affected by facial paralysis is variable (7 to 22 mm) and averages 14 mm.[37] Importantly, in our study, we saw no deficits in oral commissure excursion on the unaffected side of the face postoperatively after cross-face nerve grafting in patients with unilateral facial paralysis. These data are reassuring that harvest of a donor facial nerve branch does not instill a deficit. The negative values of improvement in commissure excursion postoperatively in the unaffected face seen in our data may reflect the effect of physical therapy in a patient's attempt to balance facial movements. Patients may learn to move the unaffected face less in an attempt to mirror the amounts of movement on the reconstructed side of the face. In a review of 47 patients with complete facial paralysis undergoing free gracilis transfer to the face neurotized with either the masseteric nerve or cross-face nerve graft, Hontanilla et al.[14] reported increased commissure displacement, contraction velocity, symmetry, and recovery in patients in the masseteric nerve group compared with the cross-face nerve graft group. Zuker and Manktelow[3] initially reported oral commissure excursion of 7 to 10 mm with use of the masseteric nerve in free gracilis transfer to the face in children with Möbius syndrome. In a study of 166 free functional muscle transfers in children, this group later reported greater amounts of commissure excursion with use of the masseteric nerve (average, 13.8 or 14.6 mm) compared with the cross-face nerve graft (7.9 mm), and these excursions approached those of the normal, unaffected side of the face (15.2 mm).[13]

Our data did not show an improvement in commissure excursion asymmetry in patients managed with the single-stage masseteric nerve technique. The majority of patients treated with the single-stage technique had bilateral facial paralysis. No facial movement bilaterally is reflected as a symmetric amount of commissure excursion preoperatively, accounting for the difference in preoperative excursion asymmetry compared with the cross-face nerve graft group. Patients with both unilateral and bilateral facial paralysis in the masseteric nerve group demonstrated minimal postoperative asymmetry in commissure excursion.

We were unable to demonstrate a qualitative correlative relationship between axon fiber number and clinical facial movement in our study, which may be because of limited power (as few patients had all data for both histomorphometry and preoperative and postoperative clinical photographs) and patient variability. Clinical differences may result from multiple variables including the time interval between reconstructive procedures and cross-face nerve graft length. The detrimental effects of absence of a muscle target on neuroregeneration continue to be described and elucidated. Less robust regeneration occurs over nerve grafts of increasing length, and part of this phenomenon may be attributable to Schwann cell denervation and/or senescence.[38–41] Similarly, long time intervals between regeneration and addition of the muscle target result in poorer functional outcomes.[40,42] A potential solution for this phenomenon has recently been suggested with end-to-side coaptations with regional sensory nerves.[43] In our study, there was variability in the timing between the two stages of the cross-face nerve graft technique, which may contribute to differences in outcome.

Analysis of clinical outcomes in facial nerve reconstruction is limited by the absence of universal, standardized outcome measures. Although global discussions regarding assessment tools continue, the Scaled Measurement of Improvement in Lip Excursion system provides a validated, reproducible, and objective measurement tool. This software is user friendly, free, and also provides the ability to analyze photographs if a patient is unable to make frequent visits to the facial nerve center. The Scaled Measurement of Improvement in Lip Excursion program is a useful adjunct to clinical facial nerve practice.

In summary, facial reanimation procedures with use of the cross-face nerve graft or masseteric nerve are effective. The masseteric nerve provides a more robust innervation source and results in greater commissure excursion. The masseteric nerve provides a reliable and effective addition to dynamic facial reconstruction.

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PATIENT CONSENT

Parents or guardians provided written consent for use of the patients' images.

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