Obturator Nerve Anatomy and Relevance to One-Stage Facial Reanimation: Limitations of a Retroperitoneal Approach

Shai Rozen, M.D.
Andres Rodriguez-Lorenzo, M.D., Ph.D.
Thorir Audolfsson, M.D.
Corrine Wong, M.D.
Angela Cheng, M.D.

Dallas, Texas; and Uppsala, Sweden

Background: Single-stage facial reanimation with a partial gracilis muscle coapted to the contralateral facial nerve seems an optimal surgical solution yet has not supplanted the two-stage approach. Insufficient obturator nerve length may limit reach to sizable contralateral facial nerve branches (possibly necessitating interposition nerve grafting), compromise optimal muscle positioning, or risk nerve coaptation under tension. This study evaluates whether retroperitoneal obturator nerve dissection would effectively lengthen the nerve, thus obviating the aforementioned limitations.

Methods: Ten hemifaces and obturator nerves of five cadavers were dissected. Facial measurements included modiolus to contralateral facial nerve branches of sufficient size at the vertical line of the lateral orbital rim. Obturator nerve measurements included gracilis neurovascular hilum to (1) obturator canal entry point (ab), (2) intraobturator canal point where additional adductor branches are inseparable by internal neurolysis (ac), and (3) retroperitoneal point of separation between anterior and posterior obturator branches (ad). Obturator nerve reach for cross-facial nerve coaptation was assessed.

Results: Successful coaptation was achieved with obturator nerve dissection to point b approximately 20 percent of the time, to point c 60 to 70 percent of the time, and to retroperitoneal point d 90 to 100 percent of the time

Conclusions: Successful coaptation to large contralateral facial nerve branches is feasible in 90 to 100 percent of cases if the entire anterior obturator branch is harvested. However, the increased risk of retroperitoneal dissection and sacrifice of additional adductor branches decreases the viability of this approach. Obturator canal dissection (point c) provides reach in 60 to 70 percent of cases, but short interposition nerve grafting may prove necessary. (*Plast. Reconstr. Surg.* 131: 1057, 2013.)

The ideal dynamic restoration of the midface in patients with facial paralysis involves attaining a dynamic, spontaneous, emotional smile, with the maximum possible symmetry in both repose and animation. The most common technique involves two stages. The first is a cross-facial nerve graft, and the second is a free muscle transfer with the motor nerve of the chosen flap, coapted to the previously placed cross-facial nerve graft. This technique has its merits and faults, which are alluded to later under Discussion.[1,2]

From the Department of Plastic Surgery, The University of Texas Southwestern Medical Center at Dallas, and the Department of Plastic and Maxillofacial Surgery, Uppsala University Hospital.
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However, if similar objectives can be met in a one-stage procedure, it would seem that the latter technique would offer several advantages: elimination of a donor nerve, shortening of the time frame until a functional smile is obtained, able to be performed in one stage, and potentially negating an additional nerve coaptation. Several one-stage techniques have been described, one of which is the use of a partial gracilis muscle flap similarly harvested for the two-stage technique with the sole difference of maximally dissecting the obturator nerve length to enable sufficient reach to the contralateral facial nerve branches. To maximize obturator nerve reach, the nerve is often dissected into the obturator canal after internal neurolysis and separation of the gracilis

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branch from the remaining anterior obturator branches innervating other thigh adductors, by means of either endoscopic or open technique.[3] To further increase nerve reach, the neurovascular hilum of the gracilis must be positioned as close as possible to the modiolus of the paralyzed side, further decreasing the distance to the contralateral facial nerve branches. Despite these surgical maneuvers, several problems may arise during surgery, mostly stemming from insufficient nerve length:

1. Inadequate nerve reach necessitating a small interposition nerve graft: This negates the advantage of one coaptation and risks a further decrease in axonal number distal to the second coaptation with possible subsequent muscle weakness.
2. Muscle malpositioning: In an attempt to increase nerve reach, the nerve hilum is placed as closely as possible to the modiolus, where placement of "muscle positioning sutures" is key to the success of the surgery. This may limit positioning of the muscle and also potentially compress the nerve along its path in the upper lip area where additional sutures are necessary for muscle positioning.
3. Compromise on recipient facial nerve branch size: Because of insufficient length of the obturator nerve, the nerve is coapted to fairly distal branches of the facial nerve rather than larger proximal branches richer in axons. An increased number of axons at the donor nerve is very likely an important factor in subsequent good muscle function.[4]

If a longer obturator nerve could be consistently harvested, possibly the above issues would be moot. Previous studies and this study show average lengths of dissection, some reaching into the obturator canal ranging from 10.6 to 13 cm.[3,5–7] These measurements still do not provide guaranteed lengths to reach larger contralateral nerve branches. Further dissection into the obturator canal may further increase the length, but even surgeons using this technique performed endoscopically describe the placement of the obturator nerve coaptation to fairly distal, small, contralateral facial nerve branches just lateral to the contralateral nasolabial fold (point y′) (Fig. 1).[5,7,8] Some authors will often verbally admit to the occasional need for nerve grafting. For the aforementioned reasons, our goal was to examine whether elongation of the obturator nerve harvest by means of

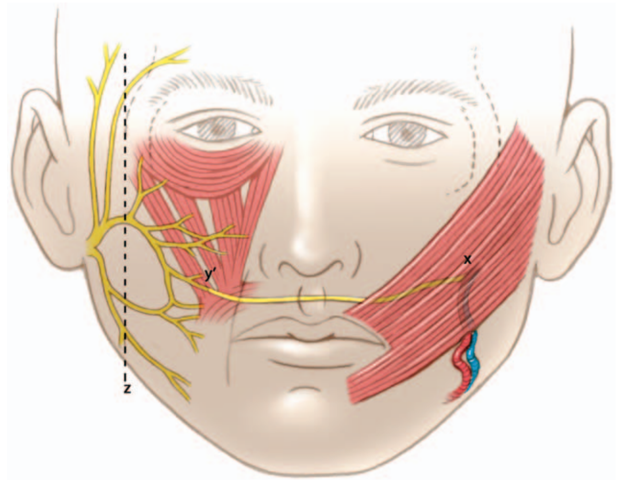

Fig. 1. One-stage reanimation with partial gracilis muscle coapted to small facial nerve branches just lateral to the contralateral nasolabial fold, as commonly described.

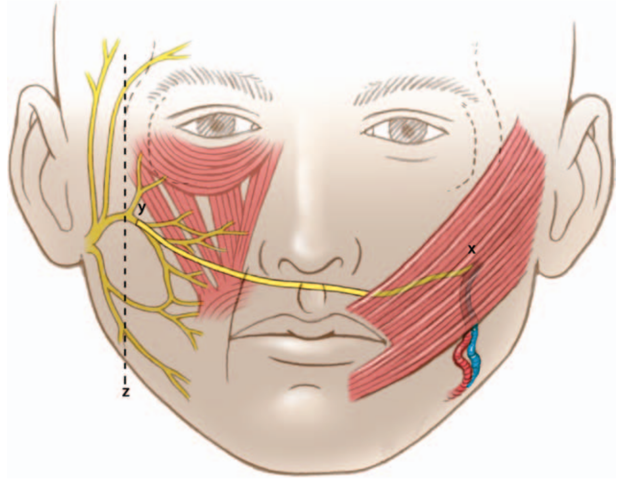

Fig. 2. One-stage reanimation with partial gracilis muscle coapted to large facial nerve branches at a vertical line correlating to the lateral orbital rim, as proposed (*x–y* denotes the distance from the gracilis muscle neurovascular hilum to the vertical line at the lateral orbital rim).

further retroperitoneal dissection will provide a practical, reproducible, and safe way to obtain sufficient nerve length to overcome these problems.

MATERIALS AND METHODS

Ten hemifaces and 10 obturator nerves were dissected in fresh cadavers. Facial measurements included distances from the modiolus (point x) (Fig. 2) to the contralateral facial nerve branches at the vertical line (line z) of the lateral orbital rim where the branches are sufficiently large (point y) (Fig. 2). The measurements were performed with a string applied on the surface of the sub–superficial musculoaponeurotic system dissection exactly where the nerve would lie and traverse from the modiolus (or where the future gracilis neurovascular hilum would approximately lie) by means of the upper lip, reaching the contralateral facial nerve branches laterally at the vertical line of the lateral orbital rim (point y) (Figs. 2 and 3).

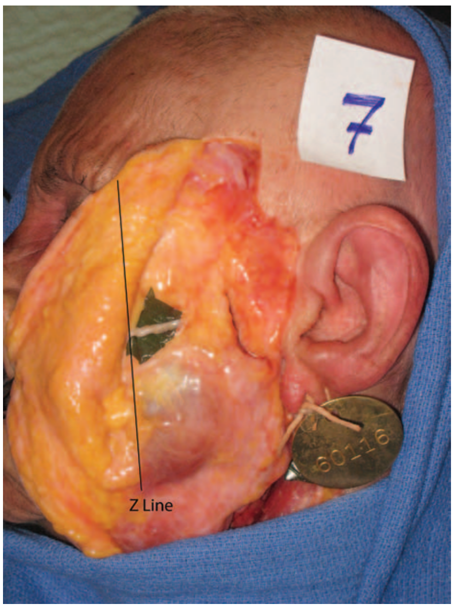

Fig. 3. Larger facial nerve branches located at the vertical line of the lateral orbital rim.

Obturator nerve measurements included three lengths, all measured from the gracilis neurovascular hilum. The first is to the entry point of the nerve into the obturator canal (a to b); the second is to the point inside the canal where the gracilis branch is inseparable by intraneural dissection from the other anterior adductor branches (a to c); the third is to the retroperitoneal point of separation of the anterior and posterior branch of the obturator nerve (i.e., the entire anterior obturator branch length) (a to d) (Fig. 4). All measurements were obtained by means of Vernier calipers (150×0.05) (Figs. 5 and 6).

RESULTS

The average length between the modiolus (on the proposed paralyzed side and where the future gracilis neurovascular hilum would approximately lie) to the contralateral facial nerve branches at the vertical line of the lateral orbital rim (x to y) was 15.2 cm (Fig. 2). The average length of the obturator nerve from the neurovascular hilum of the gracilis muscle to the entry of the obturator canal (a to b) was 12.9 cm (range, 11.0 to 14.8 cm). The average length of the obturator nerve hilum to the point in the obturator canal where intraneural dissection was not further possible (a to c) was 14.7 cm (range, 13.2 to 16.1 cm). This additional average dissection

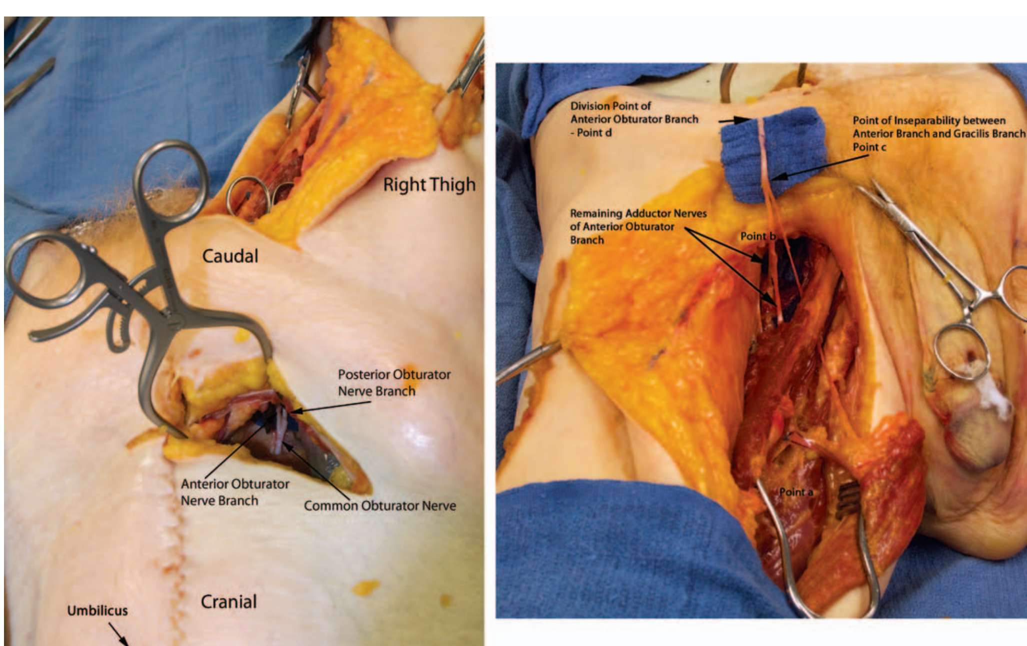

Fig. 4. (*Left*) Retroperitoneal point of separation between anterior and posterior obturator nerve branches (point *d*). (*Right*) Anterior branch of the obturator nerve. *a*, Neurovascular hilum; *b*, point of entry into obturator canal; *c*, point of nerve inseparability by internal neurolysis; *d*, division of anterior and posterior obturator branches in the retroperitoneum.

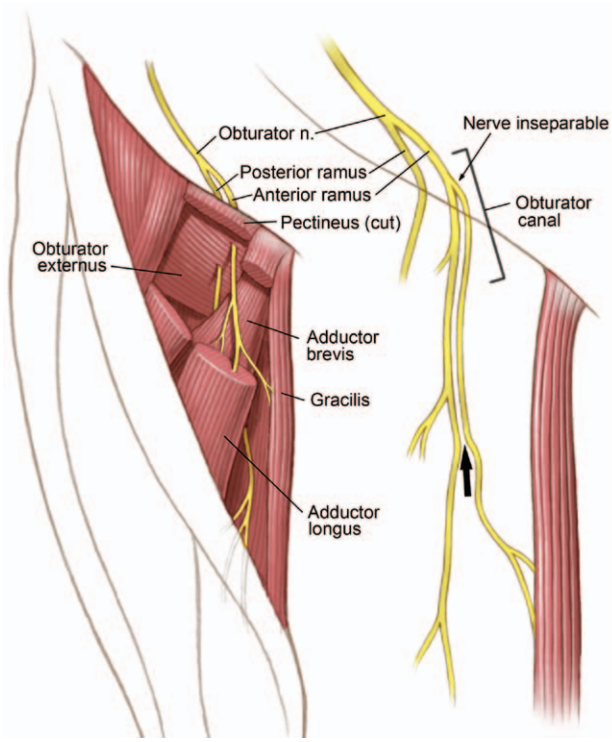

Fig. 5. Measurements of obturator nerve segments: hilum to obturator canal entry (a to b); hilum to point within the obturator canal where further intraneural dissection is not possible (a to c); full anterior obturator nerve branch length (a to d).

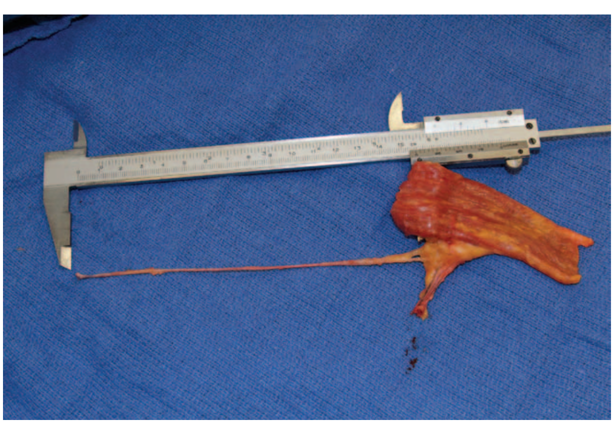

Fig. 6. Fully dissected anterior obturator branch with partial gracilis muscle flap.

(b to c) added 1.8 cm, comprising 15.0 percent elongation. The average added length of the obturator nerve obtained by dissection from the latter point (c) to the point of division of the obturator nerve into the anterior and posterior branches (d) by means of a retroperitoneal dissection was 2.9 cm (c to d), thus adding a 39.0 percent increase in nerve length compared with dissection limited to the entry of the obturator canal. No significant differences in length were seen between the right and left obturator nerves. When comparing measurements within the same cadavers between the modiolus to the vertical line of the lateral orbital rim (x to y), where contralateral facial nerve branches are large, to obturator nerve lengths from the gracilis muscle neurovascular hilum to the point of entry into the obturator canal (a to b), comfortable coaptation is attained in 20 percent of cadavers. Additional dissection into the obturator canal to a point where intraneural dissection of adductor branches is not further possible (c) provides comfortable, tension-free coaptation in approximately 60 to 70 percent of the cases without the need for an interposition nerve graft. If adductor branches are sacrificed and further retroperitoneal dissection is performed, harvesting the anterior branch in its entirety to the point of division from the posterior branch (a to d), the nerve will reach in 90 to 100 percent of cases (Tables 1 and 2).

DISCUSSION

The goal of midface reconstruction in the patient with a paralyzed face is to obtain symmetry in repose and animation; create an emotional and spontaneous smile; and, although not the primary goal, often improve speech, decrease drooling, and improve nasal breathing on the paralyzed side. Traditionally and most commonly, reconstruction is performed in two stages, consisting initially of a cross-facial nerve graft followed by a second-stage free muscle transfer 6 to 12 months later. Despite good and fairly reproducible results obtained with the two-stage procedure, the search to obtain similar results in a shorter time frame with one stage continues, thus free nerve-muscle transfers concomitantly coapted to a recipient contralateral facial nerve during the first and single stage. Several such one-stage techniques have been described, including the use of a latissimus dorsi muscle, rectus abdominis muscle, rectus femoris muscle, extensor digitorum brevis muscle, and partial gracilis muscle, each with its proponents and objective pros and cons.[8–11]

One neuromuscular flap of particular interest to this study is the partial gracilis with an extended obturator nerve length. This flap, also most commonly used in the two-stage technique, has several advantages: it allows minimal donor-site morbidity, it may be readily trimmed to size both in width and thickness, it provides good excursion, the neurovascular pedicle can be positioned in variable positions on the flap based on which facial recipient vessels are used, and it enables easy simultaneous dissection in a two-team approach.

Table 1. Average Facial Measurements (right and left) from the Modiolus to Large Facial Nerve Branches at a Vertical Line Corresponding to the Lateral Orbital Rim

	Specimen 1	Specimen 2	Specimen 3	Specimen 4	Specimen 5	Average Length
Average length, cm	13.3	14.7	17.2	16.3	14.9	15.2

Table 2. Obturator Nerve Segment Measurements*

Obturator Segment	Specimen 1	Specimen 2	Specimen 3	Specimen 4	Specimen 5	Average Length
Gracilis hilum to obturator foramen entry (a–b), cm	13.5	11.7	11	13.4	14.8	12.9
Gracilis hilum to point of inseparability in obturator canal (a–c), cm (%)	14.0 (4)	15.5 (32)	13.2 (20)	16.1 (21)	14.9 (1)	14.7 (15)
Total length of anterior obturator nerve branch (a–d), cm (%)	15.7 (16)	16.7 (43)	17.7 (61)	20.4 (53)	17.8 (20)	17.6 (39)

*Percentages represent percentage increase in length by further dissection.

Considering that both the single-stage and two-stage techniques use the same neuromuscular flap that is coapted to the contralateral facial nerve, thus providing a simultaneous, spontaneous, and emotional smile, with the sole difference that the one-stage technique would necessitate a longer obturator nerve, and that the one-stage technique can deliver the reconstructive goal in a significantly shorter time, it would be expected that the one-stage technique would have supplanted the two-stage technique or at least become more popular.

So why did this not occur? Why has the one-stage gracilis neuromuscular flap technique not become more popular? A brief comparison of the advantages and disadvantages of each technique and review of available clinical data may help understand this question but fails to provide a clear answer.

Comparison of Techniques

Two-stage technique:

Advantages:

1. A time-proven technique in both children and adults.
2. Some data suggest that symmetry in repose is better than in one-stage techniques.
3. Sufficient nerve length enables optimal positioning of the muscle.

Disadvantages:

1. Prolonged waiting time from first surgery to effective motion.
2. Minimum of two operations.
3. Often weaker excursion on reconstructed side.
4. Potential donor-site morbidity from sural nerve harvest.
5. Potential for less optimal results in older patients in there seventh to eighth decades, although the literature on this issue is scant.

One-stage gracilis neuromuscular transfer technique:

Advantages:

1. Shorter waiting time from surgery to effective motion.
2. One procedure.
3. No potential donor nerve complications (if bridging nerve graft is not needed).

Disadvantages:

1. Most authors report a need for contralateral nasolabial skin incision.
2. Coaptation to small contralateral facial nerve branches because of insufficient obturator nerve length.
3. Less symmetry in repose compared with the two-stage technique (possibly because of muscle malposition or prolonged innervation time of the muscle).
4. Possible need for bridging nerve graft if obturator nerve length is insufficient to reach sizable facial nerve branches.
5. Coaptation of obturator nerve to facial nerve under tension in cases of borderline sufficient obturator nerve length.
6. Compromise in gracilis muscle positioning to provide reach or tension-free coaptation to the contralateral facial nerve.
7. Potentially unfit for the pediatric population in which the head/face-to-limb ratio may be higher than in adults, rendering the obturator nerve insufficient in length.

The clinical data also fail to provide a clear answer as to why the technique did not gain popularity but suggest some differences in resting tone when the one-stage technique was used. In the only clinical series comparing one-stage gracilis neuromuscular transfer to the two-stage technique, the differences reported were earlier muscle activity in the one-stage technique but improved resting tone and symmetry in the two-stage technique.[5] Other one-stage techniques using different muscles report earlier recovery of muscle as the main difference and advantage over the two-stage procedure.[9]

Multiple basic science experiments comparing one-stage and two-stage techniques have been performed, and a detailed discussion of this body of work is well beyond the scope of this article, but they also fail to clearly demonstrate the advantages and disadvantages of a one-stage versus a two-stage technique. For readers interested in more detail, a bibliography is provided.[12–23]

As evidenced above, the current clinical and experimental data do not provide a clear answer as to which technique is preferable, and it is also evident that the surgeon has no control over the physiology of nerve regeneration and muscle function. The potential advantages of a one-stage technique may be counterbalanced by a potential negative effect of prolonged muscle denervation time, but conclusive evidence is lacking. Still, if the one-stage technique would reliably enable coaptation to large contralateral facial nerve branches, enable tension-free coaptation, permit optimal muscle positioning, and consistently avoid the need for a nerve graft and thus avoid a second suture line, perhaps then the single-stage technique would gain more ground and tip the pendulum in its favor. To achieve this, a consistently long obturator nerve is needed. Previous studies and this study show average lengths of dissection, some reaching into the obturator canal ranging from 10.6 to 13 cm.[3,5–7]

According to our current findings, if the nerve is dissected to the obturator canal, the nerve would reach large facial nerve branches in only 20 percent of the cases; it would reach in 60 to 70 percent of the cases if dissection were performed in the obturator canal to the point where intraneural dissection of the other adductor branches is not possible. Therefore, the goal of this study was to evaluate whether a retroperitoneal dissection would permit sufficient nerve length without increased risk from the dissection. Based on these measurements, the only way to reach large contralateral facial nerve branches consistently in approximately 90 percent of cases would be to reach the area of division between the anterior and posterior obturator nerve branches, forcing sacrifice of the adductor branches of the anterior division, potentially weakening thigh adduction and increasing risks associated with a retroperitoneal dissection. Thus, reaching large contralateral facial nerve branches, avoiding muscle malpositioning, or avoiding tension on nerve coaptation will not always be achievable without the use of nerve grafts.

With all of the above said, one should refrain from concluding that a one-stage technique with a partial gracilis neuromuscular free tissue transfer is not recommended. This study was designed merely to answer a clinical question as to whether a retroperitoneal approach for extending the obturator nerve length for a one-stage procedure is a viable option.

This study arguably has limitations. The vertical line at the lateral orbital rim was chosen based on intraoperative findings that demonstrate large facial nerve branches at this area but certainly is not a definitive point and more so is not proven to correlate to an axonal count over 900. However, this point is lateral to a point described in the one-stage techniques, which are presumed to create good excursion.

Also, sufficiently large branches may be found medially, and on rare occasions, branches at the chosen vertical may be of insufficient size, necessitating lateral parotid dissection. These small yet very realistic changes in distances may change the percentages quoted in the study significantly.

In addition, facial and obturator nerve measurements were averaged between sides, and despite the lack of statistical length difference between sides, there are slight length variances. Thus, there may be instances in which the obturator nerve of one side would provide adequate length and the contralateral obturator nerve would not. Unfortunately, preoperative obturator nerve length assessment is not possible.

Rather, one should know the limitations of dissection in which distances in individual patients may vary and therefore be prepared for nerve grafting if needed (this may not be as detrimental as thought based on a good one-stage versus two-stage comparative animal study using interposition nerve grafting by Ursa-Baiarda and Grobbelaar).[23] The technique may also be especially advantageous in two unique subgroups of patients. The first group consists of Bell palsy patients with a partially recovered facial nerve who demonstrate fair symmetry in repose but no effective motion, thereby negating the supposed disadvantage of the one-stage technique that provides decreased symmetry in repose compared to the two-stage technique.[5] This advantage would not be seen in Bell palsy patients with complete paralysis or in those with extreme muscle contractions. The second group consists of skull base tumor patients who have undergone nerve grafting procedures at the time of tumor resection, occasionally presenting with fair symmetry in repose but lacking functional animation. One should never compromise muscle positioning or perform nerve coaptation under tension.

CONCLUSIONS

Based on measurements performed in this study, dissection of the anterior branch of the obturator nerve to the obturator canal point of entry will provide sufficient length in only 20 percent of the cases if sizable recipient facial nerve branches are used at the area of a vertical line from the lateral orbital rim. Added dissection into the obturator canal may increase such successful coaptation to 60 to 70 percent of cases. Further retroperitoneal dissection of the obturator nerve to the divergence point of the anterior and posterior obturator branches increases the chances of coaptation to approximately 90 percent but not without risk. The need for a retroperitoneal dissection and, furthermore, the potential need to sacrifice additional adductor nerve branches of the anterior obturator nerve decreases the viability of this approach. Still, the one-stage approach may constitute a viable option, especially in patients presenting with baseline symmetry in repose but lacking animation, with acknowledgement that short interposition nerve grafting may be needed.

Shai Rozen, M.D.
1801 Inwood Road
Dallas, Texas 75390
shai.rozen@utsouthwestern.edu

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REFERENCES

1. Manktelow RT, Tomat LR, Zuker RM, Chang M. Smile reconstruction in adults with free muscle transfer innervated by the masseter motor nerve: Effectiveness and cerebral adaptation. *Plast Reconstr Surg.* 2006;118:885–899.
2. Bae YC, Zuker RM, Manktelow RT, Wade S. A comparison of commissure excursion following gracilis muscle transplantation for facial paralysis using a cross-face nerve graft versus the motor nerve to the masseter nerve. *Plast Reconstr Surg.* 2006;117:2407–2413.
3. Rodríguez Lorenzo A, Morley S, Payne AP, Tollan CJ, Soutar DS. Anatomy of the motor nerve to the gracilis muscle and its implications in a one-stage microneurovascular gracilis transfer for facial reanimation. *J Plast Reconstr Aesthet Surg.* 2010;63:54–58.
4. Terzis JK, Wang W, Zhao Y. Effect of axonal load on the functional and aesthetic outcomes of the cross-facial nerve graft procedure for facial reanimation. *Plast Reconstr Surg.* 2009;124:1499–1512.
5. Kumar PA, Hassan KM. Cross-face nerve graft with free-muscle transfer for reanimation of the paralyzed face: A comparative study of the single-stage and two-stage procedures. *Plast Reconstr Surg.* 2002;109:451–462; discussion 463.
6. Kumar PA. Cross-face reanimation of the paralysed face, with a single stage microneurovascular gracilis transfer without nerve graft: A preliminary report. *Br J Plast Surg.* 1995;48:83–88.
7. Ashayeri M, Karimi H. One-stage reversed and rotated gracilis muscle free flap for chronic facial palsy: A new technique. *Plast Reconstr Surg.* 2002;110:1298–1302.
8. Guelinckx PJ, Sinsel NK. Muscle transplantation for reconstruction of a smile after facial paralysis past, present, and future. *Microsurgery* 1996;17:391–401.
9. Harii K, Asato H, Yoshimura K, Sugawara Y, Nakatsuka T, Ueda K. One-stage transfer of the latissimus dorsi muscle for reanimation of a paralyzed face: A new alternative. *Plast Reconstr Surg.* 1998;102:941–951.
10. Yang D, Morris SF, Tang M, Geddes CR. A modified longitudinally split segmental rectus femoris muscle flap transfer for facial reanimation: Anatomic basis and clinical applications. *J Plast Reconstr Aesthet Surg.* 2006;59:807–814.
11. Mayou BJ, Watson JS, Harrison DH, Parry CB. Free microvascular and microneural transfer of the extensor digitorum brevis muscle for the treatment of unilateral facial palsy. *Br J Plast Surg.* 1981;34:362–367.
12. Aydin MA, Mackinnon SE, Gu XM, Kobayashi J, Kuzon WM Jr. Force deficits in skeletal muscle after delayed reinnervation. *Plast Reconstr Surg.* 2004;113:1712–1718.
13. Frey M, Koller R, Liegl C, et al. Role of a muscle target organ on the regeneration of motor nerve fibres in long nerve grafts: A synopsis of experimental and clinical data. *Microsurgery* 1996;17:80–88.
14. Koller R, Rab M, Todoroff BP, et al. The influence of the graft length on the functional and morphological result after nerve grafting: An experimental study in rabbits. *Br J Plast Surg.* 1997;50:609–614.
15. Lundborg G, Dahlin LB, Danielsen N, et al. Nerve regeneration across an extended gap: A neurobiological view of nerve repair and the possible involvement of neuronotrophic factors. *J Hand Surg Am.* 1982;7:580–587.
16. Mackinnon SE, Dellon AL, Hunter DA. Histological assessment of the effects of the distal nerve in determining regeneration across a nerve graft. *Microsurgery* 1988;9:46–51.
17. O'Brien BM, Pederson WC, Khazanchi RK, Morrison WA, MacLeod AM, Kumar V. Results of management of facial palsy with microvascular free-muscle transfer. *Plast Reconstr Surg.* 1990;86:12–22; discussion 23.
18. Politis MJ, Ederle K, Spencer PS. Tropism in nerve regeneration in vivo: Attraction of regenerating axons by diffusible

factors derived from cells in distal nerve stumps of transected peripheral nerves. *Brain Res.* 1982;253:1–12.

19. Rab M, Haslik W, Grünbeck M, et al. Free functional muscle transplantation for facial reanimation: Experimental comparison between the one- and two-stage approach. *J Plast Reconstr Aesthet Surg.* 2006;59:797–806.
20. Rab M, Koller R, Haslik W, et al. The influence of timing on the functional and morphological result after nerve grafting: An experimental study in rabbits. *Br J Plast Surg.* 2002;55:628–634.
21. Taylor GI. Nerve grafting with simultaneous microvascular reconstruction. *Clin Orthop Relat Res.* 1978;133:56–70.
22. Taylor GI, Ham FJ. The free vascularized nerve graft: A further experimental and clinical application of microvascular techniques. *Plast Reconstr Surg.* 1976;57:413–426.
23. Urso-Baiarda F, Grobbelaar AO. A comparison of one- versus two-stage surgery in an experimental model of functional muscle transfer with interposed nerve grafting. *J Plast Reconstr Aesthet Surg.* 2009;62:1042–1047.

Plastic Surgery Level of Evidence Rating Scale—Prognostic/Risk Studies

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