Facial Nerve Monitoring During Cerebellopontine Angle and Skull Base Tumor Surgery: A Systematic Review from Description to Current Success on Function Prediction

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Key words
- Cerebellopontine angle surgery
- Direct electrical stimulation
- Electromyography
- Facial motor evoked potential
- Facial nerve
- Intraoperative monitoring
- Skull base surgery

Abbreviations and Acronyms
- CMAP: Compound muscle action potentials
- CN: Cranial nerves
- CPA: Cerebellopontine angle
- DES: Direct electrical stimulation
- EMG: Electromyography
- FMEP: Facial motor evoked potential
- FN: Facial nerve
- IAC: Internal auditory canal
- IOFNM: Intraoperative facial nerve monitoring
- MUP: Motor unit potential
- SEP: Somatosensory evoked potential
- TES: Transcranial electrocorticostimulation
- VS: Vestibular schwannoma

BACKGROUND: Intraoperative neuromonitoring has been established as one of the methods by which modern neurosurgery can improve surgical results while reducing morbidity. Despite routine use of intraoperative facial nerve (FN) monitoring, FN injury still is a complication of major concern due to severe negative impact on patient’s quality of life.

METHODS: Through searches of PubMed, we provided a systematic review of the current literature up to February, 2011, emphasizing all respects of FN monitoring for cerebellopontine angle and skull base tumor surgery from description to current success on function prediction of standard and emerging monitoring techniques.

RESULTS: Currently, standard monitoring techniques comprise direct electrical stimulation (DES), free-running electromyography (EMG), and facial motor evoked potential (FMEP). We included 62 studies on function prediction by investigating DES (43 studies), free-running EMG (13 studies), and FMEP (6 studies) criteria. DES mostly evaluated postoperative function by using absolute amplitude, stimulation threshold, and proximal-to-distal amplitude ratio, whereas free-running EMG used the train-time criterion. The prognostic significance of FMEP was assessed with the final-to-baseline amplitude ratio, as well as the event-to-baseline amplitude ratio and waveform complexity.

CONCLUSIONS: Although there is a general agreement on the satisfactory functional prediction of different electrophysiological criteria, the lack of standardization in electrode montage and stimulation parameters precludes a definite conclusion regarding the best method. Moreover, studies emphasizing comparison between criteria or even multimodal monitoring and its impact on FN anatomical and functional preservation are still lacking in the literature.

INTRODUCTION
The aims of surgery in the cerebellopontine angle (CPA) have changed from tumor resection and prolongation of life to the anatomical and functional preservation of the cranial nerves (CNs) (80, 162). This evolution in surgical therapy may be precisely illustrated by Moskowitz and Long (127), who divided the surgical treatment of vestibular schwannomas (VS) into 4 distinct phases, namely the pioneer era (1890 to 1925), the curative era (1925 to 1960), the magnification era (1960 to 1974), and the recent era (from 1975). Although significant advances have been observed in the recent era, facial nerve (FN) anatomical preservation during VS surgery is currently around the range of 95% and FN functional preservation is in the low range of 70%.

FN injury is not exclusively related to VS surgery and may also occur postoperatively in several tumors of the CPA. For instance, the meningiomas of the CPA have a common anatomical location and are classified according to their site of tumor origin in relationship to the internal auditory canal (IAC). The tumors may arise anterior to IAC (group 1), involve the IAC (group 2), or may grow superior to the IAC (group 3), inferior to the IAC (group 4) or posterior to the IAC (group 5) (132). The operative strategies and functional facial and cochlear nerve outcomes are different among the groups (132, 188). Immediate postoperative facial paresis can be observed in 13% to 23.7% depending on the tumor location (132). Management of CPA epidermoid tumors has improved during the past 30 years; however, postoperative facial weakness still occurs in 5% to 8.3% of patients (155, 161). Similarly, trigeminal neurenomas remain challenging entities, and their surgical treatment may lead to postoperative facial paralysis in up to 37.5% of cases (160). Therefore, in general, facial weakness is still a complication of major con-
cern in patients undergoing CPA surgery (6, 9, 35, 49, 52, 57, 95, 159, 185).

Dealing with CPA tumors has developed from almost a death sentence at the beginning of the 20th century (80, 87, 142, 158) to the current concept of functional microsurgery (157). In this interim, several developments regarding radiological diagnosis, the introduction of the operative microscope and microsurgical techniques, advances in the field of neuroanesthesia, as well as intraoperative neuromonitoring were responsible for significant reductions in the morbidity and mortality in patients suffering from CPA tumors (35, 37, 41, 52, 53, 55, 57, 61, 71, 72, 77, 79-81, 87, 95, 117, 127, 131, 137, 142, 158, 163, 176, 180, 186). In this report, we review the current literature emphasizing all aspects of FN monitoring for CPA and skull base tumor surgery from description to recent success on function prediction of standard and emerging monitoring techniques.

METHODS

The PubMed database was searched for publications through February 2011 using the MeSH terms “facial nerve”, “intraoperative monitoring”, “cerebellopontine angle”, and “skull base”. The search included articles in the English, German, and French languages. All reference sections were manually reviewed and pertinent articles identified. Initially, relevant articles were retrieved in either title or abstract format and full-text manuscripts were subsequently collected for all original articles related to current study. FN monitoring during otological, neurological, facial hemispasm, and head and neck surgeries were primarily excluded unless abstract information was considered relevant to the present study.

RESULTS AND DISCUSSION

Historical Background

Intraoperative monitoring of the FN is not a new concept per se (80); Dr. Fedor Krause (92), on July 14, 1898, described the use of monopolar FN stimulation during a cochlear nerve section for intractable tinnitus and reported his findings, as follows:

The divided acusticus was now placed backward, so that it came in contact with the cerebellum. Unipolar faradic irritation of the remaining nerve trunk with the weakest possible current of the induction apparatus resulted in contractions of the right facial region, especially of the orbicularis oculi, as well as of the branches supplying the nose and the mouth. The irritation of the displaced acusticus (using also the very weakest possible current), caused the right shoulder to be elevated twice in succession. The accessory situated below had undoubtedly been reached by the current, because it was, together with the stump of the acusticus, bathed in liquor that had trickled down.

with this description, Krause not only reported the first use of FN monitoring but also anticipated the enduring problem of current spread (203). Similar techniques were developed during the following years; however, Givré and Olivecrona in 1949 (53) introduced a significant advance by using a special nurse to observe the patient’s face beneath sterile drapes. Givré and Olivecrona (53) even advocated surgery under local anesthesia because facial function could be assessed throughout the procedure. In addition, they were possibly the first to direct attention to the assessment of postoperative function prediction. After tumor resection, the function of the FN was tested either by voluntary function or faradic stimulation (53). During the 1960s, Hilger (64), Jako (72), and Parsons (141) devised FN stimulators for parotid and ear surgery. Jako’s device was unique because of a motion detector that was placed inside the patient’s mouth and alerted the surgeon with an audible signal in response to facial movements (72, 80). This method has surpassed the first “acoustic” FN monitoring performed by “facial nerve protectors,” in which surgical assistants “shouted” to the surgeon whenever a facial movement was observed [Miehlke 1964, cited by Prass and Lüders (148)].

The technique of observing the patient’s face for visible contractions remained the state of the art for FN identification until the late 1970s (35, 145, 203). In 1979, Delgado et al. (35) introduced the use of intraoperative electromyographic (EMG) surface electrodes for FN monitoring during CPA surgeries to improve identification and to facilitate the dissection of the FN. In 1982, Sugita and Kobayashi (185) modified this technique by using a new device that consisted of a pair of accelerometers attached to the orbicularis occuli and oris that converted facial movements into audible sounds through a loudspeaker to provide acoustic feedback to the surgeons. Thereby the surgeons were able to recognize facial responses without the necessity of having a member of the surgical staff observing the patient’s face (185). Sugita and Kobayashi (185) also documented a false-positive error due to an inadvertent stimulation of the trigeminal nerve, in which the patient had the FN sectioned because of the misjudgment. Moller and Jannetta (123, 124) introduced the next refinement by developing a system that combined the acoustic monitoring of spontaneous EMG activity and EMG activity in response to electrical stimulation. Thereafter, Prass and Lüders (148) and Prass et al. (147) correlated and classified the specific patterns of EMG and acoustic activities as the result of surgical manipulations.

The Impact of Intraoperative Monitoring on the Anatomical and Functional Preservation of the FN

For many years, FN function had been evaluated by means of electrical stimulation and monitoring the visible and palpable activity of the facial muscles during surgery in the posterior fossa, temporal bone, and parotid gland, as well as monitoring the evoked activity with electrical recordings (62). However, demonstration of the improvement in FN anatomical and functional preservation by using intraoperative facial nerve monitoring (IOFNM) was not assessed until 1987. Harner et al. (62) retrospectively compared 48 monitored patients, matched by age, tumor size, and most recent year of operation, to unmonitored patients. Similar overall FN anatomical preservation rates were observed, 88% in the monitored group and 79% in the unmonitored group. Nevertheless, differences were most striking when patients were subclassified by tumor size so that in patients with large tumors the FN anatomical preservation rates improved from 37% in the unmonitored group to 67% in the monitored group (62). For small and medium-sized tumors, no difference was noted in the immediate postoperative period, although there were more patients affected with total loss of function in the unmonitored group (62).

That study was updated thereafter, including 91 patients with the same method-
operative (37). Kwartler et al. (93) retro-preserved an excellent facial function post-operatively (37). Harner et al. (61) thereby concluded that IOFM demonstrated an increased ability to preserve the FN with less postoperative deformity and stated, “I don’t think I could convince anybody at our institution with experience to give up monitoring under any circumstances.”

Niparko et al. (137) studied retrospectively 29 monitored and 75 unmonitored patients affected by VS. Testing the results for the subgroups revealed that monitoring was significantly associated with satisfactory facial function 1 year postoperatively for patients harboring large tumors (>2 cm), whereas for smaller tumors the better results in the monitored group did not achieve statistical significance. Leonetti et al. (100) investigated the advantages of IOFM during the infratemporal approach by analyzing 31 unmonitored versus 20 monitored patients. Normal postoperative FN function was increased from 70% in the unmonitored patients to 92% in the monitored patients. In addition, none of the monitored patients developed severe facial palsy postoperatively (100, 101). In a historical cohort, Hammerschlag and Cohen (60) compared 111 consecutively monitored patients with 207 previously unmonitored patients. The overall rate of complete facial palsy decreased from 14.5% to 3.6% in the monitoring group.

Dickins and Graham (37) evaluated the postoperative results of 108 patients stratified into 3 groups, namely: group 1 had no facial monitoring (38 patients), group 2 was monitored using a motion-type detector system (29 patients), and group 3 was monitored by means of an EMG system (41 patients). Normal facial function or slight facial dysfunction was encountered in 39% of the patients in the unmonitored group and in 55% of the motion detector group, whereas 87% of the EMG monitored group preserved an excellent facial function post-operatively (37). Kwatal et al. (93) retrospectively reviewed the FN function of 155 unmonitored and 89 monitored patients. The monitored large-sized tumor group showed significantly better functional results at the immediate postoperative period and at discharge (93). At the long-term follow-up, no statistical difference was noted, although there remained a trend toward better results in the monitored group (93).

The results are sound but should be interpreted with care because of the problematic issue of comparing studies due to the lack of standardization in FN grading and distribution of tumor sizes (37). Moreover, it should be remembered that regardless of the monitoring technique, IOFM is merely a technical adjunct that can aid both the experienced and the inexperienced surgeon and does not replace surgical skills and experience (15, 16, 37, 72, 77, 80, 95, 141, 172, 174, 185). Nevertheless, monitoring may have a special educational role by refining the surgeons’ technique in order to favor sharp over blunt dissection, which is known to produce more EMG activity (80, 191), as Kartush (77) stated: “... monitoring appears to be an outstanding teacher which molds the techniques of young surgeons by providing important feedback during dissection. Thus, monitoring reinforces the essence of microsurgical technique. . . .”

Because the National Institutes of Health Consensus Statement on Acoustic Neuroma (1) explicitly recommended routine use of IOFM, there have been no formal clinical trials to assess the benefits of surgery with monitoring over surgery without monitoring (202, 203). The studies that have emerged thereafter in the literature have maintained the same concepts of retrospective data evaluation, although clear benefits in the quality of the postoperative facial function may be observed in monitored patients, not only in those affected by VS (94, 125, 131, 139, 173, 179, 199), but also in patients suffering from other CPA and skull base conditions (98, 110, 111).

Overall studies indicate that there is an improvement in FN outcome by using IOFM, especially in large tumors (44, 62, 74, 77, 79-81, 83, 85, 98, 101, 104, 110, 111, 121, 123, 125, 131, 137, 138, 147, 148, 169, 177, 179, 199, 207). Thus, intraoperative neuromonitoring has been established as one of the methods in which modern neurosurgery can improve surgical results while reducing morbidity (77, 156), although a controlled, prospective, randomized study is still lacking until now (80, 165). Such a study is unlikely to be enrolled because most surgeons who have included monitoring in their practice believe that there is indeed a benefit and are reluctant to withdraw intraoperative monitoring from their patients (77, 79, 80). Furthermore, IOFM may also improve hearing preservation outcomes because of the likelihood of reducing surgical trauma that may jeopardize both nerves (61, 63, 77, 80).

The Objectives of Intraoperative FN Monitoring

The main purpose of intraoperative monitoring is to make the surgical team aware of the ongoing changes in the neural function, thereby permitting modifications in surgical strategies that can ultimately avoid neural damage (77, 79). Effective neurophysiologic monitoring requires knowledge of pertinent anatomy and physiology; selection of the appropriate monitoring techniques based on the structures at risk for each surgical procedure; and appropriate interpretation of the evoked responses based on knowledge of the normal activity (77, 80). Thus, the objectives of IOFM include (76, 77, 80, 137, 140, 172, 173, 202, 203):

1. Identifying precociously the FN in soft tissue, tumor, and bone;
2. Warning the surgeon of an unexpected facial stimulation;
3. Mapping the course of the FN in the temporal bone or tumor by using electrical stimulation;
4. Enhancing neural preservation by reducing mechanical trauma to the FN during rerouting or tumor dissection;
5. Assessing the prognosis of the FN function at the end of tumor removal.

Achieving these goals demands the use of various monitoring techniques that are now available. Standard FN monitoring techniques during CPA and skull base surgery include direct electrical stimulation (DES) and free-running EMG (189). Alternative FN monitoring techniques have been devised mostly by taking advantage of the antidromic and orthodromic properties of motor nerve excitation after peripheral
stimulation (27-29, 153, 167, 193-197). These techniques have the advantage of being used in patients anesthetized with neuromuscular blocking agents and monitoring of the entire nerve with a single electrode (203). Although interesting results have been reported from these studies (27-29, 153, 167, 193-197), the lack of transsynaptic conduction, that is, the absence of the brainstem component, corresponds to the major limitation of antidromic and orthodromic potentials because a complete section of the FN at CPA may be associated with little or no changes in response amplitude (76, 144). This is due to the preservation of the nerve electrical excitability peripheral to the injury site that takes some days to disappear (24, 25, 47, 141). Moreover, the sensitivity of these techniques to nerve injury is still unclear so far, and nerve potentials cannot be converted into audible signals to provide immediate feedback to surgeons (137, 203). Nevertheless, further investigations should be encouraged (203).

Technical Considerations

Types of Stimuli. Electrical stimulation is conventionally performed by applying rectangular pulses delivered by 2 electrodes, namely the cathode that becomes negative and the one that becomes positive, which is called the anode (73). The basic parameters for a rectangular pulse are intensity and pulse duration, measured in milliamperes and milliseconds, respectively (73). The stimulation of the nerve depends on the amount of charge (coulombs) delivered, which is the product of the amount of current (current intensity) and the amount of time of current application (pulse duration) (73, 169). In practical means, it is worth noting that for a comparison among studies, not only should the current delivered be considered, but also the pulse duration. In this way, a charge delivered to a nerve using a 0.2-mA stimulation threshold with 50 μs of pulse duration is equivalent to 0.1 mA when a 100-μs pulse duration is applied (169).

Types of Stimulators

Two types of stimulators are commercially available, the constant-current and the constant-voltage stimulators (73). Constant-current stimulators maintain the current intensity at a desired level, whereas constant-voltage stimulators maintain a constant voltage between electrodes (73). The strength of the stimulus may then be measured in milliamperes or in volts (141). Thus, the current delivered to the tissues is related directly to the voltage, and inversely to the resistance by Ohm’s law (amplitude = voltage/resistance) (141).

Constant-current stimulators are used in most neurophysiological studies due to their consistent response (73, 123). Møller and Jannetta (123) have described constant-voltage stimulation with the assumption that most of the current applied flows through lower-impedance fluids instead of through the nerve. Therefore by using a constant-current device the current intensity should be raised to a higher level to obtain an adequate response (123). In this way, if the fluid is suddenly removed or if the nerve becomes exposed, the higher current then comes in direct contact with the nerve, with potentially damaging consequences (123, 202, 203).

On the other hand, Prass and Lüders (146) have demonstrated no practical advantage of constant-voltage over constant-current stimulation by using a flush-tip probe (a stimulation probe that is insulated to the tip), and advocated the use of the constant-current device because the amount of current delivered is not affected by the diameter of the stimulation probe. These results were further confirmed by Kartush et al. (81), indicating that constant-current sources can be effectively used with the insulation of the stimulating probes. In addition, stimulus artifacts, especially current shunting, may be minimized when bipolar electrodes are used along with flush-tip insulation probes (81, 146).

Additionally, by using constant-voltage stimulators the current delivered changes with tissue resistance and therefore may be erratic and unsuitable for quantitative evaluations and signal averaging (73). Therefore, their use should be restricted to FN identification during surgeries in the posterior fossa (73). The use of constant-current or constant-voltage stimulators is still a matter of debate so that future studies, especially experimental, are necessary and should be dedicated to solving this controversy definitively (203).

Types of Stimulation Probes. Although 2 electrodes are always necessary to produce electrical stimulation, monopolar stimulation is defined in such situations where only 1 active electrode is in close contact to the stimulated tissue, while the reference electrode is placed far from the target tissue (73, 136). Monopolar and bipolar stimulation probes have been used in several studies (203). The current density is better distributed in monopolar probes, representing an advantage of this method. This leads to a direct correlation between the stimulus strength and the obtained responses (73). Current spreading is a major problem inducing false-positive responses by causing the activation of any tissue, especially the CNs, lying along the current pathway (35, 50, 63, 73, 79, 81). These responses may be minimized by placing the reference electrodes far from the target tissue, especially in directions not traversed by other nerves, and by using a larger reference electrode in relation to the active electrode (73).

Bipolar stimulation is considered when both electrodes are active and placed in close contact with the stimulated tissue (73, 136). The electrodes can be configured side by side, as a bayonet forceps, or concentrically (73). This type of stimulation shows more specificity and precision in localization because it tends to stimulate mainly the tissue under or in between the 2 electrodes, thus reducing the likelihood of current spreading to a distant reference electrode (61-63, 73, 79, 81, 203). Moreover, the tip orientation of bipolar electrodes can produce changes in amplitude responses (14, 73, 81). Interestingly, longitudinal placement of the electrodes over the nerve axis requires one-half to two-thirds of the current intensity that is required when electrodes are positioned orthogonally or across the nerve axis (73, 81). Limitations of bipolar stimulation comprise the complexity of its current distribution and current shunting to cerebrospinal fluid or blood collections leading to false-negative responses (63, 73, 123). Compared with bipolar probes, monopolar electrodes require a current intensity 2 to 3 times higher to reach the same responses (81).

The best stimulation protocol is a continuous source of debate (81, 202, 203). Although Møller and Jannetta (123) have demonstrated some advantages of constant voltage over constant current, their study compared monopolar voltage with bipolar current. However, depending on the desired clinical goals, variations of protocols may be necessary to optimize the effect of monitoring (137). Owing to significant differences in the electrical characteristics of monopolar and bipolar probes, some inves-
tigators recommend concurrent use of both probes based on the specific clinical goals (81). Thus monopolar stimulation can be utilized in tumor mapping when high sensitivity is indispensable, whereas the bipolar configuration is most suitable for CN differentiation within the CPA considering its high specificity and low current requirements (10, 77, 79, 81, 121, 168, 173).

**Types and Placement of Recording Electrodes.** Surface, subcutaneous needle, and monopolar or bipolar intramuscular hook wire electrodes can be used for EMG recording (63, 172, 202, 203). Wire electrodes have the highest impedance and the lowest field of view; the subdermal needles have intermediate impedance and a large field of view; whereas surface electrodes have the lowest impedance and the largest field of view (168).

Surface electrodes are time consuming to use, less specific, susceptible to artifacts, and easily displaced during surgery (172, 202, 203). For these reasons they are considered inadequate for EMG monitoring (63, 172). Conversely, hook wire electrodes, although advocated by some investigators due to their high sensitivity and specificity for detecting muscular responses (14, 63, 115, 123, 148), have no major practical advantage and may be more traumatic to the skin and muscles (203). Therefore, electro-encephalography platinum needle electrodes are the most commonly used because of their large uninsulated surface compared with single-fiber EMG electrodes and their ability to identify specific muscle activity anywhere within the target muscle (203).

Initial studies of facial EMG used a single recording channel to monitor both the superior and the inferior branches of the FN by placing 1 electrode of the bipolar configuration in each of the orbicularis oculi and orbicularis oris (123). This range montage, however, is more vulnerable to artifacts because of the wider separation between the electrodes, and to impairments in response recognition to DES during sustained EMG activity (203). Multichannel recordings have overcome both limitations because of the likelihood increase of having at least 1 channel free of ongoing EMG activity, allowing adequate DES even during EMG irritation (203). In addition, multichannel electrode montage increases the sensitivity of EMG recordings (21, 58). It is thus recommended to monitor at least 2 branches of the FN by using 2 recording channels (2 electrodes of the bipolar configuration for each of the superior and inferior branches of the FN) (203) placed at least 5 mm apart (152), as described by Kartush et al. (79).

The placement of recording electrodes is not so far standardized, being arbitrarily applied over the facial muscles (59). Kartush et al. (79) recommend close paired electrode application in the orbicularis oculi muscle and at the nasolabial groove. Considering that placement of recording electrodes may contribute to the magnitude of muscle responses (59) thereby impairing the quality of monitoring and consequently the detection of EMG pathological activity (152), Guo et al. investigated optimal placement of recording electrodes around the eye and lip (59). Based on their results, it was concluded that consistent recordings were obtained by using the following configuration: for the orbicularis oris muscle, electrodes should be 1.5 cm apart by the orbital rim just below the eyebrow and at the lateral canthus; whereas for the orbicularis oris muscle, electrode 1 is inserted 2 cm away from the oral commissure and the second electrode may be placed 1 cm apart within either the superior or inferior lip because the montages did not show any statistical difference (59).

In addition to EMG recordings, devices based on motion detectors for the facial muscles may be useful adjuncts because of the limitation of EMG-based techniques for FN monitoring during electrocautery (63, 172, 191). The created artifacts that occur concurrently to cautery jeopardize adequate identification of EMG responses that might indicate FN damage from thermal injury (203). As a result, there is an increased risk of FN injury during this particular surgical step (203). In spite of the several motion detectors (15, 72, 128, 171, 174, 175, 185, 191, 192, 211) and even the video-based systems (32, 45, 49, 129, 130) that have been developed, EMG recordings remain the most sensitive indicator of FN activation (15, 37, 46, 147, 172, 175, 203). During posterior fossa surgeries, EMG recordings require lower current levels to be activated and react earlier than an audio alarm (15, 37). Furthermore, the elicitation of evoked EMG responses that might correspond to FN injury are detected in the EMG monitor without producing facial movements that sound the audio alarm (15). It should be noted, however, that no device allows adequate monitoring during electrocautery (76).

**Anesthesia.** FN EMG monitoring can be performed under essentially all types of anesthetic regimens, with the exception of neuromuscular blocking agents, which might hinder the accuracy of IOFNM by interfering with propagation of potentials that might be incompatible with appropriate EMG monitoring (137, 203). Nonetheless, some studies have demonstrated that even under moderate to profound levels of peripheral neuromuscular blockade, it is possible to elicit facial EMG activity either by DES or mechanical manipulation without compromising FN monitoring (20, 22, 65, 99). The assumption is that facial muscles are somehow insensitive to neuromuscular blocking agents (20, 22). This phenomenon is not entirely understood, although a different type of innervation (a greater number and size of neuromuscular junctions) and a lower affinity of acetylcholine receptors in the facial muscles to acetylcholine are suggested as potential explanations (20, 22).

Further studies in a large patient series should be performed to confirm these findings. Moreover, chronically injured FN, as in the case of CPA diseases, may present a greater sensitivity to lower levels of neuromuscular blockade (20). For now, there is a general belief that even a partial blockade compromises spontaneous and mechanically evoked activities, and thus its use should not be recommended for FN monitoring (14, 81, 203). Short-acting agents, namely succinylcholine, may be administered during tracheal intubation because it is expected to be cleared during the surgical approach, returning to normal status before the critical stages of the surgery have been reached (63, 79, 203).

**DES**

IOFNM with electrical stimulation has become a widely used technique during CPA surgeries (13). The use of DES is very simple in its concept (79). A stimulating probe is used to apply DES over the posterior fossa structures and to generate the compound muscle action potentials (CMAP) that are recorded through paired electrodes placed on the patient’s face in the ipsilateral facial muscles, whereas a
ground electrode is positioned at the forehead (79) (Figure 1). The response of the facial muscles is monitored acoustically through a loudspeaker, and the magnitude of the muscle contractions is visually observed on the monitor (13, 14). It is important to recognize that the stimulus intensity required to evoke CMAPs is higher in injured nerves or nerve roots (65, 175). DES may be used as an adjunct during surgical exploration within the anatomical regions traversed by FN, providing real-time information about the nerve status (13, 54, 141). The safety of nerve stimulation has been well established, in both animal models (67, 68) and clinical practice (16, 81, 169).

Intraoperative Use. Tumors arising in the CPA and temporal bone may displace, attenuate, or even encase the FN in a way that its identification may be cumbersome (81). In smaller tumors, FN identification and confirmation is straightforward with DES (203). But frequently, especially in larger tumors, the only way to locate the nerve appropriately is by using DES (203). Precise FN location is the first step toward preservation of function (16).

Therefore, FN identification is thus the primary utility of DES (54, 203) and the most adequate technique for mapping (54, 79).

Regardless of the stimulation protocol (whether bipolar versus monopolar probes or constant-current versus constant-voltage stimulators), FN location is determined by using higher charges (usually between 0.3 to 1 V or 0.1 to 3 mA) within the CPA, the temporal bone, as well as the tumor surface (95, 115, 116, 169, 173, 178, 203). Generally, stimulation is more easily obtained when the nerve is located close to the electrode rather than far from the stimulating probe (73) but if the current is too high, monopolar probes will permit current spreading from tissues to FN (173, 204, 205). Herein, it is important to recognize that by using stimulation intensities of about 0.5 to 0.6 mA, the current spread is dispersed within a maximum of 2 cm from the electrode (204). Furthermore, approximately 1 mA of current is equivalent to 1 mm of temporal bone covering the FN (173-175).

Within the posterior fossa, however, a smaller current is usually necessary to stimulate the exposed FN (generally 0.1 to 0.2 mA) (173). Stimulation of the trigeminal motor fibers may produce EMG activity in the facial muscle channels due to considerable crosstalk between channels (15, 203). Differentiation can be accomplished by their different waveforms, namely smaller amplitude and shorter latencies observed with trigeminal EMG responses (204). The activation of trigeminal motor fibers typically produces EMG responses in 2 to 4 ms, whereas facial responses are obtained rather late in 5 to 8 ms (97, 190, 203, 204). After nerve identification, the stimulus intensity is reduced to minimize current spreading, which may be set at the lowest intensity required to elicit an evoked EMG response (35, 116, 178). FN stimulation is then performed throughout the surgical procedure to confirm nerve location and integrity (35).

Before tumor resection, the tumor capsule should be stimulated to confirm whether there are any FN fibers in the area to be dissected (35, 172, 203). If no responses are obtained even when using high charges, then it is assumed that the FN is far from the stimulating area, therefore dissection can proceed more rapidly without risking the FN (81, 172, 203). This is particularly useful in VS because a posterior position of
the FN can be rarely found in approximately 3% of the patients (164, 181), although the nerve typically runs through the anterior superior or anterior middle portion of the tumor capsule in VS (23, 164). In this way, DES helps to avoid sectioning an aberrant course or splayed nerve that may be positioned in the posterior capsule of the tumor (172).

Additional warning of unexpected FN stimulation has gained some interest recently after a description of nerve splitting, which may be frequently recognized, especially in medial arising VS (124, 181, 182). FN splitting occurs in approximately 36% of medial VS and is recognized by selective stimulation (181). In this situation, the FN has 2 portions, 1 major branch located on the anterior middle part of the tumor capsule and 1 minor branch that runs over the cranial tumor pole (181, 182). Stimulation of the smaller branch evokes responses exclusively on the orbicularis oris muscle (182). The selectivity of evoked responses gives rise to the assumption of a topographical arrangement of the FN fibers within the CPA (182). Ashram et al. (10), on the other hand, attributed the same electrophysiological results of long-latency, low-amplitude EMG responses recorded only on the orbicularis oris channel to the stimulation of the nervus intermedius. This recognition has the same surgical impact regardless of whether or not this smaller branch is considered the nervus intermedius (182), due to the likely protection of the FN from inadvertent sectioning by indicating that the main trunk of the nerve is located in an entirely different location within the CPA (10, 182).

Function Prediction. After the completion of the tumor removal, the facial function is evaluated (79, 97, 172, 203, 206). To assess postoperative facial function, several protocols of FN stimulation were devised using a wide variety of stimulation sources, stimulator electrode designs, placement and types of recording electrodes, and IFNM criteria (69, 70, 169, 203, 206). A detailed description of the published studies of the function prediction of DES is summarized in Table 1. Intraoperative information based on the results of DES would permit the surgeon to give the patient an immediate assessment with regard to the likely FN function (176). Additionally, accurate and early prediction of both FN injury and FN recovery may allow adequate planning for the best management, including earlier procedures of facial reanimation before significant facial muscle atrophy has developed (11, 69, 70, 85, 186). On the other hand, a correct function prediction may also avoid unnecessary surgical procedures while function recovery is still likely (42).

Amplitude of Evoked CMAP. The introduction of the absolute amplitude value of the contraction of the facial muscles after tumor removal as a predictor parameter was proposed initially by Harner et al. (61). Thereafter, Beck et al. (13) have quantified the magnitude of muscle contraction in response to 0.05 mA of stimulation at the brainstem. CMAP amplitude is directly proportional to the number of stimulated muscle fibers (169), thereby reflecting the number of intact axons (54, 63, 205). Interestingly, the absolute CMAP values at the IAC remain relatively constant throughout the procedure, but those over the root exit zone (REZ) usually decrease as the surgery proceeds (116, 201, 204, 205). This observation may demonstrate a fairly temporal relationship between progressive nerve damage and surgical manipulation, ultimately indicating a loss of conducting axons from intraoperative injury (63, 205). The major limitation of this method comprises the wide interindividual variability because of the inconsistency in needle position and the size of the monitored muscles among patients (169). This is reflected by a great threshold variation among the published studies. Some studies consider CMAP amplitude from 100 to 500 μV in response to 0.05 to 0.6 mA of brainstem stimulation as the cutoff value for a compromised postoperative facial function (8, 13, 135, 178, 205). Thus, patients demonstrating a reduced amplitude in muscle contractions are correlated with impaired postoperative facial function (13, 17, 61). Maximal or near-maximal stimulation would render larger CMAPs, but the risk of electrical injury would be unnecessarily increased (169).

Stimulation Threshold. For activating the FN, the minimal amount of stimulation is usually sought so that the best conducting fibers respond (169). The stimulus threshold is achieved by finding the electrical threshold necessary to produce an EMG recording. If a response is obtained, this is evidence of an intact anatomical and functional FN (61). The lack of standardization of the techniques and parameters precludes a detailed analysis among published results (169, 203). However, there is a trend toward predicting good postoperative function by applying low-threshold stimulation at the brainstem after tumor resection, especially lower than 0.05 to 0.1 mA (21, 82, 176) or 0.1 V (114), whereas elevated thresholds of levels as high as 2 to 3 mA (85, 175) or 1 to 3 V are commonly associated with severe facial dysfunction (66, 203).

A large prospective study was recently concluded indicating a less optimistic interpretation of the 0.05-mA criteria (184). Sughrue et al. (184) identified that an elevated stimulation threshold (>0.05 mA) was highly specific but also insensitive for function prediction, therefore suggesting that the predictive value of such criteria remains to be determined. It is worth emphasizing that the stimulating protocol provided a real current of 0.1 mA due to 200 μs of pulse duration (184), as discussed earlier.

Proximal-to-Distal Amplitude Ratio. Together with the introduction of EMG surface electrodes for the accurate recording of evoked responses, Delgado et al. (35) also suggested stimulation at both the IAC and the REZ to assess postoperative facial function at the end of tumor resection. As a result, both absolute CMAP amplitudes were used to confirm nerve integrity so that similar amplitudes were correlated to facial weakness with rapid function recovery, whereas amplitude reduction between the REZ and the IAC was associated with longstanding facial weakness (35). The extent of the axonal damage is therefore estimated by using the relative amplitude ratio (62).

Proximal-to-distal amplitude ratio eliminates the interindividual variability of each response that is found with other electrophysiological techniques of function prediction (188). Therefore, this method is believed to be more accurate than the abovementioned (188). Besides stimulating the FN at distal IAC and REZ the role of DES is extended to the detection and quantification of conduction block (188). Although these findings were not corroborated by Benecke et al. (16), overall studies considering the ratio criteria for predicting the FN outcome indicate that there is indeed an improvement in function prediction when compared to absolute amplitude and stimulation threshold (6, 17, 54, 62, 69, 186, 205).

A proximal-to-distal amplitude ratio >30% is a strong indicator of good to excel-
<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design</th>
<th>Number of Patients</th>
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<th>Pulse (µs)</th>
<th>Protocol (CC/CV)</th>
<th>Probe</th>
<th>Channels, Muscle</th>
<th>Stimulation Site</th>
<th>IOFNM Criteria</th>
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</thead>
<tbody>
<tr>
<td>Delgado et al., 1979 (35)</td>
<td>Retro</td>
<td>14</td>
<td>VS</td>
<td>50</td>
<td>CV</td>
<td>Mono</td>
<td>1, frontalis</td>
<td>IAC, REZ</td>
<td>Absolute CMAP amplitude at both sites (0 to 30 V)</td>
<td>Similar amplitude confirmed gross integrity of FN Decreased amplitude between IAC and REZ in 2 cases that had mild and severe facial palsy</td>
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<tr>
<td>Harner et al., 1987 (62)</td>
<td>Retro</td>
<td>48</td>
<td>VS</td>
<td>50</td>
<td>CV</td>
<td>Bipo</td>
<td>1, 2 to 4 (oculi, oris, mentalis, masseter, or temporalis); 1, surface</td>
<td>IAC, REZ</td>
<td>Relative CMAP amplitudes on both sites (10 to 50 V)</td>
<td>Mild reduction (&lt;50%), moderate (&gt;50%) or no proximal response was strongly correlated with postoperative facial dysfunction</td>
</tr>
<tr>
<td>Harner et al., 1988 (61)</td>
<td>Retro</td>
<td>91</td>
<td>VS</td>
<td>50</td>
<td>CV</td>
<td>Bipo</td>
<td>1, oculi or oris, mentalis, masseter, temporalis; 1, surface</td>
<td>IAC, REZ</td>
<td>Any response to stimulation (from 10 V); if the proximal response is low, distal stimulation (IAC) to define extent of lesion</td>
<td>If a response is observed, this means intact FN Low CMAP response, definite increase in facial weakness</td>
</tr>
<tr>
<td>Silverstein et al., 1988 (175)</td>
<td>Retro</td>
<td>301</td>
<td>Ot, VS</td>
<td>200</td>
<td>CC</td>
<td>Mono</td>
<td>NA, oris (motion detector)</td>
<td>REZ</td>
<td>&gt;0.3 mA stimulation at the end of tumor resection</td>
<td>Facial weakness is expected if &gt;3 mA, facial palsy is likely to occur</td>
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<tr>
<td>Niparko et al., 1989 (137)</td>
<td>Retro</td>
<td>29</td>
<td>VS</td>
<td>100</td>
<td>CC</td>
<td>Bipo</td>
<td>NA</td>
<td>IAC, REZ</td>
<td>Equal proximal and distal response at the end of tumor resection</td>
<td>67%, HB I at 1 week 88%, HB I at 1 year</td>
</tr>
<tr>
<td>Beck et al., 1991 (13)</td>
<td>Retro</td>
<td>56</td>
<td>VS</td>
<td>100</td>
<td>CC</td>
<td>Mono</td>
<td>1, oris</td>
<td>REZ</td>
<td>1. 500 µV amplitude of neurotonic discharge (trains) sustained for ≥30s 2. 500 µV amplitude of orbicularis oris response using 0.05 mA stimulation at the end of tumor resection</td>
<td>Four groups of patients: A. &lt;500 µV EMG and &gt;500 µV to stimulation B. &gt;500 µV EMG and to stimulation C. &lt;500 µV EMG and to stimulation D. &gt;500 µV EMG and &lt;500 µV to stimulation Group A, at 1 week, 97% had HB grade I</td>
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<td>Kirkpatrick et al., 1991 (86)</td>
<td>Retro</td>
<td>18</td>
<td>CPA</td>
<td>1000</td>
<td>CC</td>
<td>Bipo</td>
<td>1, oris</td>
<td>NA</td>
<td>Any response to 0.5–1.0 mA stimulation (up to 5 mA)</td>
<td>Small tumor, 73% had HB I/II at 3 to 43 mo Large tumor, 43% had HB III/V at 3 to 43 mo</td>
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<td>Study</td>
<td>Study Design</td>
<td>Number of Patients</td>
<td>Histology</td>
<td>Pulse (µs)</td>
<td>Stimulus Protocol (CC/CV)</td>
<td>Probe</td>
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<td>Berges et al., 1993 (17)</td>
<td>Retro</td>
<td>43</td>
<td>VS</td>
<td>NA</td>
<td>CC</td>
<td>Mono</td>
<td>2, oris, oculi</td>
<td>IAC, REZ</td>
<td>A ratio was calculated by using the minimal stimulation threshold (I) and the induced amplitude EMG response (A) in the CPA (R = I/A) and IAC (R = I/A) R = R / R</td>
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<td>R &lt; 2, 90% HB I/II at 10d</td>
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<td>Kirkpatrick et al., 1993 (85)</td>
<td>Retro</td>
<td>26</td>
<td>VS</td>
<td>1000</td>
<td>CC</td>
<td>Both</td>
<td>2, oculi, oris</td>
<td>REZ</td>
<td>≤2 mA stimulation after tumor resection</td>
<td>67%, HB I/II at 6 to 43 mo</td>
</tr>
<tr>
<td>Prasad et al., 1993 (145)</td>
<td>Retro</td>
<td>34</td>
<td>CPA</td>
<td>100 to 200</td>
<td>CV</td>
<td>NA</td>
<td>2, oculi, oris</td>
<td>REZ</td>
<td>Pre vs. post tumor resection variation =0.2 V of proximal stimulation</td>
<td>90%, HB I/II at 2 d 83%, HB I/II at 1 to 44 mo</td>
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<tr>
<td>Wolf et al., 1993 (201)</td>
<td>Pros</td>
<td>25</td>
<td>VS</td>
<td>100</td>
<td>CC</td>
<td>Mono</td>
<td>3, tumor side, 1, opposite side</td>
<td>REZ</td>
<td>1. 500 µV amplitude of neurotonic discharge (trains) sustained for ≥30s 2. 500 µV amplitude of muscle response using 0.1 to 0.4 mA stimulation at the end of tumor resection</td>
<td>Response &lt;500 µV EMG and &gt;500 µV to stimulation was correlated with normal facial function in 90% of the patients at 1 day</td>
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<tr>
<td>Lacombe et al., 1994 (94)</td>
<td>Retro</td>
<td>62</td>
<td>VS</td>
<td>100</td>
<td>CC</td>
<td>Mono</td>
<td>2, oculi, oris</td>
<td>REZ</td>
<td>≤0.1 mA, All HB I/II at 1 mo  Between 0.1 and 0.3 mA, 71.4% HB I/II at 1 mo &gt;0.3 mA, 20% HB I/II at 1 mo</td>
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<tr>
<td>Lalwani et al., 1994 (95)</td>
<td>Retro</td>
<td>129</td>
<td>VS</td>
<td>200</td>
<td>CV</td>
<td>Mono</td>
<td>2, oculi, oris</td>
<td>REZ</td>
<td>≤0.2 V stimulation after tumor resection</td>
<td>Stimulation threshold was not correlated with immediate postoperative 98%, HB I/II at 1 y, if &gt;0.2 V, 50% HB I/II</td>
</tr>
<tr>
<td>Lenarz and Ernst, 1994 (98)</td>
<td>Retro</td>
<td>30</td>
<td>CPA</td>
<td>100</td>
<td>CC</td>
<td>Both</td>
<td>2, oculi, oris</td>
<td>REZ</td>
<td>Significantly increased in patients with postoperative facial weakness (0.73 mA) indicating poor outcome and long-lasting nerve damage</td>
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</table>

**Table 1. Continued**

**Study Design**
- Retro: Retrospective
- Pros: Prospective

**Number of Patients**
- VS: Variable
- CPA: Constant

**Histology**
- NA: Not applicable

**Pulse (µs)**
- CC: Constant
- CV: Variable

**Stimulus Protocol (CC/CV)**

**Probe**
- Mono: Monopolar

**Channels, Muscle**
- IAC, REZ: Intracranial, retromastoid

**Stimulation Site**
- REZ: Retromastoid

**IOFNM Criteria**
- A ratio was calculated by using the minimal stimulation threshold (I) and the induced amplitude EMG response (A) in the CPA (R = I/A) and IAC (R = I/A) R = R / R

**Results**
- R < 2, 90% HB I/II at 10d
- ≥2 mA stimulation after tumor resection
- 67%, HB I/II at 6 to 43 mo
- 90%, HB I/II at 2 d 83%, HB I/II at 1 to 44 mo
- Response <500 µV EMG and >500 µV to stimulation was correlated with normal facial function in 90% of the patients at 1 day
- ≤0.1 mA, All HB I/II at 1 mo  Between 0.1 and 0.3 mA, 71.4% HB I/II at 1 mo >0.3 mA, 20% HB I/II at 1 mo
- ≤0.2 V stimulation after tumor resection
- Stimulation threshold was not correlated with immediate postoperative 98%, HB I/II at 1 y, if >0.2 V, 50% HB I/II
- Significantly increased in patients with postoperative facial weakness (0.73 mA) indicating poor outcome and long-lasting nerve damage
<table>
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<tr>
<td>Maurer et al., 1994 (116)</td>
<td>Retro</td>
<td>35</td>
<td>VS</td>
<td>100</td>
<td>CC</td>
<td>Both</td>
<td>2, oculi, oris</td>
<td>REZ</td>
<td>Relative EMG amplitude reduction of more than 50% after tumor resection in comparison to before resection</td>
<td>More frequent poor outcomes in patients with relative amplitude reduction</td>
</tr>
<tr>
<td>Silverstein et al., 1994 (176)</td>
<td>Retro</td>
<td>44</td>
<td>VS</td>
<td>200</td>
<td>CC</td>
<td>Mono</td>
<td>NA (EMG), oris (motion detector)</td>
<td>REZ</td>
<td>≤0.1 mA stimulation after tumor resection (EMG or motion detector)</td>
<td>95%, HB I/II at ≥1 ylf between 0.1 to 0.2 mA, 82% HB I/II</td>
</tr>
<tr>
<td>Yokoyama et al., 1994 (205)</td>
<td>Retro</td>
<td>52</td>
<td>VS</td>
<td>100</td>
<td>CC</td>
<td>Mono</td>
<td>NA</td>
<td>IAC, REZ</td>
<td>Mean EMG amplitude to stimulation over the REZ (&gt;100 μV) or percentage of EMG amplitude between REZ and IAC (&gt;30%) with 0.5–0.6 mA stimulation</td>
<td>Good or excellent outcome at 6 to 24 mo</td>
</tr>
<tr>
<td>Maurer et al., 1995 (115)</td>
<td>Retro</td>
<td>102</td>
<td>CPA, skull base</td>
<td>100</td>
<td>CC</td>
<td>Both</td>
<td>2, oculi, oris</td>
<td>REZ</td>
<td>Relative EMG amplitude reduction of more than 50% after tumor resection in comparison to before resection</td>
<td>More frequent poor outcomes in patients with relative amplitude reduction</td>
</tr>
<tr>
<td>Taha et al., 1995 (186)</td>
<td>Retro</td>
<td>20</td>
<td>VS</td>
<td>100</td>
<td>CC</td>
<td>Mono</td>
<td>2, oculi, oris</td>
<td>Distal IAC, REZ</td>
<td>Proximal-to-distal CMAP amplitude ratio with lowest stimulation intensity (0.05–0.1 mA)</td>
<td>Ratio &gt;2/3, all patients with HB III or better immediately postoperative and HB I at 14–28 moRatio 1.3 / &lt;2.3, 90% HB III or worse immediately postoperative and 100% HB III or better at final follow-up Ratio &lt;1/3, all patients with HB IV or worse at immediate and at final follow-up</td>
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<tr>
<td>Selesnick et al., 1996 (169)</td>
<td>Retro</td>
<td>49</td>
<td>CPA</td>
<td>50</td>
<td>CC</td>
<td>Mono</td>
<td>NA, multich</td>
<td>REZ</td>
<td>≤0.1 mA stimulation after tumor resection</td>
<td>93%, HB I/II at 1 ylf between ≤0.2 mA, 78% HB I/II</td>
</tr>
<tr>
<td>Hone et al., 1997 (66)</td>
<td>Pros</td>
<td>27</td>
<td>VS</td>
<td>100</td>
<td>CC</td>
<td>Bipo</td>
<td>2, frontalis, oris</td>
<td>REZ</td>
<td>Lowest current to elicit &gt;250 μV for facial muscle contraction</td>
<td>Stimulus threshold &gt;0.1 mA, HB &gt;2 immediately postoperative and 6 mo</td>
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<th>Stimulation Site</th>
<th>IOFNM Criteria</th>
<th>Results</th>
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<tr>
<td>Magliulo and Zardo, 1997 (112)</td>
<td>Retro</td>
<td>23</td>
<td>Skull base</td>
<td>NA</td>
<td>CC</td>
<td>Mono</td>
<td>2, oculi, oris</td>
<td>IAC, REZ</td>
<td></td>
<td>1. Ongoing train activity and muscle contraction to stimulation (Beck method, 1991) 2. Ratio between IAC and REZ (Berges method, 1993) 3. Stimulation threshold (Silverstein method, 1994) Borges and Silverstein methods showed better sensitivity Ratio of the evoked amplitude response predicted the facial function in 91.3% of the patients at 1 y Stimulation threshold correctly predicted the facial function in 86.9% Beck method failed to predict postoperative facial function</td>
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<tr>
<td>Nissen et al., 1997 (138)</td>
<td>Retro</td>
<td>81</td>
<td>VS</td>
<td>NA</td>
<td>CV</td>
<td>Mono</td>
<td>NA</td>
<td>IAC, REZ</td>
<td></td>
<td>Minimal voltage stimulus to elicit an EMG response (stimulus threshold) Median threshold of 0.1 V, HB I/II at 6 mo Median threshold of 0.725 V, HB III/IV at 6 mo</td>
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<tr>
<td>Zeitouni et al., 1997 (207)</td>
<td>Pros</td>
<td>109</td>
<td>VS</td>
<td>NA</td>
<td>CC</td>
<td>Mono</td>
<td>2, oculi, oris</td>
<td>REZ</td>
<td></td>
<td>1. Minimal current stimulus to elicit an EMG response (stimulus threshold) Intraoperative thresholds significantly associated with immediate and late follow-up, 87% threshold between 0.05–0.1 mA (HB/I II 83% at immediate and 91.6% at 1 y) CMAP amplitude failed to predict facial function</td>
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<tr>
<td>Mandpe et al., 1998 (114)</td>
<td>Pros</td>
<td>44</td>
<td>VS</td>
<td>NA</td>
<td>CV</td>
<td>Mono</td>
<td>2, oculi, oris</td>
<td>IAC, REZ</td>
<td></td>
<td>1. Stimulation threshold (≤0.1 V) 2. CMAP amplitude (0.2 V above threshold) 3. Threshold + CMAP amplitude ≤0.1 V, 74% HB I/II at discharge CMAP amplitude ≥200 µV, 89% HB I/II at discharge Low threshold + high amplitude, 88% HB I/II at discharge The use of FN threshold + amplitude is a better predictor than threshold alone</td>
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<td>Study</td>
<td>Study Design</td>
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<td>Magliulo and Zardo, 1998 (113)</td>
<td>Retro</td>
<td>34</td>
<td>VS</td>
<td>NA</td>
<td>CC</td>
<td>Mono</td>
<td>2, oculi, oris</td>
<td>IAC, REZ</td>
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<td>Ongoing train activity and muscle contraction to stimulation (Beck method, 1991)</td>
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<td>3. Stimulation threshold (Silverstein method, 1994)</td>
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<tr>
<td>Sobottka et al., 1998 (178)</td>
<td>Retro/pros</td>
<td>60</td>
<td>VS</td>
<td>100</td>
<td>CC</td>
<td>Mono</td>
<td>2, oculi, oris</td>
<td>REZ</td>
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<td>1. Proximal and distal absolute CMAP amplitude (0.05–0.1 mA)</td>
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<td>3. Proximal-to-distal CMAP amplitude ratio</td>
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<td>Axon and Ramsden, 1999 (11)</td>
<td>Pros</td>
<td>184</td>
<td>VS</td>
<td>200</td>
<td>CC</td>
<td>Bipo</td>
<td>2, oculi, oris</td>
<td>Proximal to the site of tumor</td>
<td>Minimal stimulation threshold (0.05 mA)</td>
<td>94% sensitivity in predicting good long-term facial function and 91% PPV</td>
</tr>
<tr>
<td>Fenton et al., 1999 (44)</td>
<td>Pros</td>
<td>35</td>
<td>VS</td>
<td>100</td>
<td>CC</td>
<td>NA</td>
<td>NA</td>
<td>Medial and lateral to tumor</td>
<td>Minimal stimulation intensity medial and lateral to tumor after tumor resection</td>
<td>Medial minimal stimulation ≤0.1 mA, 96% HB I/II immediately postoperative ≥0.15 mA, 30% HB I/II, is suggestive of an abnormal facial function</td>
</tr>
<tr>
<td>Study</td>
<td>Study Design</td>
<td>Number of Patients</td>
<td>Histology</td>
<td>Pulse (μs)</td>
<td>Pulse Protocol (CC/CV)</td>
<td>Probe</td>
<td>Channels, Muscle</td>
<td>Stimulation Site</td>
<td>IDFNM Criteria</td>
<td>Results</td>
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<tr>
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<tr>
<td>Goldbrunner et al., 2000 (54)</td>
<td>Pros</td>
<td>137</td>
<td>VS</td>
<td>100</td>
<td>CC</td>
<td>Bipo</td>
<td>2, oculi, oris</td>
<td>Distal IAC, REZ</td>
<td>Proximal-to-distal CMAP amplitude ratio with lowest stimulation intensity (0.5 mA)</td>
<td>Ratio &gt;0.8, 1.6% risk of severe facial weakness at 6 mo Ratio &lt;0.1, 75% risk of severe facial weakness at 6 mo Absolute CMAP amplitude values reached statistical significance only for subgroups (HB IV/V)</td>
</tr>
<tr>
<td>Fenton et al., 2002 (42)</td>
<td>Pros</td>
<td>67</td>
<td>VS</td>
<td>100</td>
<td>CC</td>
<td>NA</td>
<td>2, oculi, oris</td>
<td>Medial to tumor</td>
<td>Minimal stimulation intensity medial and lateral to tumor after tumor resection</td>
<td>0.1 mA, 88% of the patients were correctly predicted to have a favorable initial outcome on the basis of tumor size and stimulation threshold</td>
</tr>
<tr>
<td>Isaacson et al., 2003 (69)</td>
<td>Retro</td>
<td>229</td>
<td>VS</td>
<td>100</td>
<td>CC</td>
<td>Mono</td>
<td>2, oculi, oris</td>
<td>IAC, REZ</td>
<td>1. Stimulus threshold 2. Proximal-to-distal CMAP amplitude ratio</td>
<td>≤0.5 mA, 93.6% HB I/II at 6 mo Ratio &gt;0.33, 97% HB I/II at 6 mo</td>
</tr>
<tr>
<td>Fenton et al., 2004 (43)</td>
<td>Prod</td>
<td>16</td>
<td>CPA non-VS</td>
<td>100</td>
<td>CC</td>
<td>NA</td>
<td>NA</td>
<td>REZ</td>
<td>Stimulation threshold &lt;0.1 mA</td>
<td>Good long-term FN outcome</td>
</tr>
<tr>
<td>Akagami et al., 2005 (6)</td>
<td>Pros</td>
<td>71</td>
<td>CPA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>2, oculi, oris</td>
<td>NA</td>
<td>Proximal-to-distal CMAP amplitude ratio</td>
<td>Independent variable predictive of satisfactory FN outcome</td>
</tr>
<tr>
<td>Anderson et al., 2005 (8)</td>
<td>Retro</td>
<td>67</td>
<td>VS (&gt;3 cm)</td>
<td>NA</td>
<td>CC</td>
<td>Mono</td>
<td>NA</td>
<td>REZ</td>
<td>Absolute CMAP amplitude &gt;100 μV in response to as high as 0.4 mA stimulation</td>
<td>93%, HB I/II at final follow-up (6 mo to 1 y)</td>
</tr>
<tr>
<td>Bozorg-Grayeli et al., 2005 (21)</td>
<td>Pros (multi)</td>
<td>111</td>
<td>VS</td>
<td>NA</td>
<td>CC</td>
<td>Mono</td>
<td>4, oculi, oris, frontalis, platysma</td>
<td>Fundus, IAC, REZ</td>
<td>Lowest intensity that elicits a response &gt;100 μV on at least 1 channel</td>
<td>&lt;0.05 mA, appeared to improve the prognostic value for predicting immediate postoperative function 0.01–0.04 mA, 93% HB I/II at day 8 0.05–0.3 mA, 85% HB I/II at day 8 &gt;0.3 mA, 79% HB I/II at day 8</td>
</tr>
<tr>
<td>Study</td>
<td>Study Design</td>
<td>Number of Patients</td>
<td>Histology</td>
<td>Pulse (μs)</td>
<td>Stimulus Protocol (CC/CV)</td>
<td>Probe</td>
<td>Channels, Muscle</td>
<td>Stimulation Site</td>
<td>IOFNM Criteria</td>
<td>Results</td>
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</tbody>
</table>
| Grayeli et al., 2005 (58)   | Pros         | 89                 | VS        | NA         | CC                         | Mono  | 4, oculi, oris, frontalis, platysma | Fundus, IAC, REZ | 1. Lowest intensity that elicits a response >100 μV on at least 1 channel | 0.01–0.04 mA, 90% HB I/II at days 1 and 8  
0.05–0.2 mA, 75% HB I/II at days 1 and 8  
>0.2 mA, 20% HB I/II |
| Neff et al., 2005 (135)     | Pros         | 74                 | VS        | NA         | CC                         | NA    | 2, oculi, oris   | REZ              | 1. Response amplitude >240 μV or greater, and  
2. Stimulation threshold 0.05 mA or less | One criterion, 85% HB I/II at 1 y  
Both criteria, 98% probability of HB I/II at 1 y  
Stimulus threshold or response amplitude alone had a lower probability with the same result |
| Isaacson et al., 2005 (70)  | Retro        | 60                 | VS        | 100        | CC                         | Mono  | 2, oculi, oris   | IAC, REZ          | 1. Stimulus threshold  
2. Proximal-to-distal CMAP amplitude ratio | Accurate in predicting increased risk of long-term FN dysfunction when a logistic regression model was used  
Score >0.8, all patients with final HB III or better  
Score <0.8, 67% do not regain eye closure |
| Lin et al., 2006 (103)      | Pros         | 38                 | VS        | 200        | CC                         | Bipo  | 3, oculi, oris, frontalis | REZ              | Percentage ratio was calculated by dividing the CMAP response to REZ stimulation (0.05–0.3 mA) by the amplitude of distal ipsilateral transcutaneous maximal stimulus response | CMAP >50% of the maximum, 93% PPV of HB I/II immediately postoperative  
CMAP >20% of the maximum, 81% PPV |
| Shamji et al., 2007 (170)   | Retro        | 127                | VS        | NA         | NA                         | NA    | NA              | NA              | Stimulation threshold | <0.1 mA, predictive of functional nerve preservation |
| Bernat et al., 2010 (19)    | Pros         | 120                | VS        | 100,000    | CC                         | Mono  | 4, oculi, oris, frontalis, chin | IAC, REZ          | 1. Stimulation threshold  
2. Response amplitude after supramaximal stimulation (2 mA), and  
3. Proximal-to-distal CMAP amplitude ratio | <0.04 mA, sens 89% and spec 43%  
CMAP amplitude >800 μV, sens 38% and spec 87%  
Ratio <0.6, sens 78% and spec 40%  
All 3 criteria, sens 90% and spec 78% to predict HB 1 or 2 at day 8 |
Table 1. Continued

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of Patients</th>
<th>Stimulation Site</th>
<th>Channels, Muscle</th>
<th>Probe</th>
<th>Stimulation Protocol (CC/CV)</th>
<th>Pulse (µs)</th>
<th>Number of Histologies</th>
<th>IOFNM Criteria</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soghi et al. (2010)</td>
<td>477</td>
<td>PROS</td>
<td>NA</td>
<td>NA</td>
<td>0.05 mA</td>
<td>200</td>
<td>VS</td>
<td>IOFNM, immediate visual feedback (PM, EL, EMG), immediate visual feedback (PM, EMG), intraoperative monitoring, NA, not attributable to surgical trauma</td>
<td>Stimulation threshold (0.05 mA)</td>
</tr>
</tbody>
</table>

The concurrent use of amplitude response and stimulus threshold, however, increases the ability of function prediction for both early and late postoperative function by reducing the rates of false-positive results when compared with stimulation threshold alone in either a constant-current or constant-voltage stimulation protocol (114, 135). Similarly, the association of stimulus threshold and proximal-to-distal ratio was also found to be beneficial, especially in predicting the final outcome for patients affected by moderate to severe postoperative facial dysfunction (60, 70). Thus, a combination of methods may provide the best predictive assessment of postoperative facial function (203).

Free-Running EMG

Continuous free-running EMG is typically monitored from paired electrodes, which are placed in the muscles innervated by nerves or nerve roots that are considered to be at risk of damage during surgical procedure (65). Actually, the concept of continuous FN monitoring to provide immediate feedback to the surgeon was introduced with acoustic devices (72, 123, 148, 171). These techniques were used to detect facial movements in response to FN mechanical trauma during surgical manipulation (16, 65, 72, 123, 147, 148, 171) (Figures 2 and 3). Accordingly, EMG recordings from several muscles can be monitored concurrently by using a loudspeaker for acoustic feedback and an oscilloscope for visual feedback (63, 79, 173). The most important type of EMG recording during surgery is the neurotonic discharge. These discharges comprise muscle unit potential activity in response to mechanical or metabolic irritation of the nerve that innervates the monitored muscles (63). Interestingly, it is worth noting that similar to triggered CMAPs, injured motor nerves are less likely to evoke neurotonic discharges after mechanical trauma (65).

Although FN preservation was improved by using acoustic monitoring, interest in analyzing the patterns of EMG activity in response to specific surgical manipulation has gained attention only with the studies of Prass and Lüders (148) and Prass et al. (147). The patterns of EMG activity were then classified into spontaneous and evoked activity (147, 148). The evoked activities correspond to the great majority of the documented in-
traoperative EMG responses that occur as a direct consequence of surgical maneuvers (147, 148). DES, mechanical trauma, and electrocautery were all related to evoked EMG activities of different amplitudes and waveforms that were further divided into bursts, trains, and pulse EMG patterns (148). In addition, the EMG patterns also differed in degree of synchrony, duration, and/or temporal relationship with the eliciting events (148).

The pulse pattern is observed after DES and is easily recognized by its pulsed audible signs in synchrony with the electrical stimulation (148). The burst pattern is the most frequently encountered EMG activity, which is characterized by short, relatively synchronous bursts of motor unit potentials that last up to a few hundred milliseconds (148). There is a direct cause-and-effect relationship between the appearance of the burst activity and the initiating events, in other words the surgical maneuvers, namely direct mechanical trauma, electrocautery, or irrigation (133, 147, 148). Interestingly, neurotonic discharges are less likely to occur after sudden laceration of the nerve (63, 76). Bursts probably arise owing to the mechanoreceptor properties or metabolic irritation of the nerve fibers resulting ultimately in the depolarization and elicitation of the action potential (63, 148). Thus, burst pattern probably corresponds to a single discharge of multiple FN axons (148). Rapid and high-frequency mechanical trauma may produce EMG bursts of greater density than slower rates of compression (148). The elicitation of burst activity is an indirect sign of a functional FN because bursts are easily obtained in healthy axons when compared with FN severely compromised by tumor involvement (63, 147, 148). Therefore, burst patterns of EMG activity are probably due to FN stimulation of several mechanisms and may not necessarily correspond to nerve injury (148). Eventually the burst pattern is followed by sustained periodic activity that lasts up to 30 seconds (148).

Finally, the train pattern is characterized by asynchronous trains of motor unit potentials with a duration of up to several minutes (147, 148). Two types of trains were identified that differ in regard to frequency, amplitude, regularity of interval, pattern of buildup, and decline of motor unit potentials (148). High-frequency trains (50 to 100 Hz) have a typical acoustic quality that resembles an airplane engine, called the bomber potentials. Low-frequency trains (1 to 50 Hz), on the other hand, render an acoustic signal that is similar to popping popcorn, with a lower occurrence than high-frequency trains (148). Train activity is mostly correlated to the surgical traction of the FN, especially when the traction occurs in a lateral-to-medial direction within the CPA (133, 147, 148). Interestingly, there is a delay from seconds to minutes between the occurrence of the provoking event and the onset of the train activity (148). Similar to the burst pattern, electrocautery, mild nerve trauma, and free irrigation may also be associated with episodes of EMG train activity, especially the bomber type, whereas the release of brain retractors and dissectors leads to a reduction in EMG activity (66, 133, 148).

Because of onset delay, establishing a direct cause-and-effect relationship between surgical manipulation and EMG responses is a difficult issue regarding train activity (148). However, the onset delay of train activity in response to lateral-to-medial traction may be explained by the compromise of arterial supply and consequent nerve ischemia (148). This results in the repetitive firing of 1 or more motor units due to maintenance of the axonal membrane potential above the level of the action potential threshold (148). Train responses are frequently observed in FN severely involved by a tumor, which becomes more susceptible to dissection and surgical traction (148). The identification of train activity may indicate potential or ongoing FN injury (popcorn type) or even significant injury (bomber type) (148).

Although a variety of audible signals and EMG patterns were described, the studies in the field had remained a continuous source of controversy (Table 2) until the year 2000, when Romstöck et al. (154) provided a detailed analysis of intraoperative EMG patterns with respect to their surgical implications. Romstöck et al. (154) identified 5 types of spontaneous EMG patterns instead of the 3 described by Prass and Lüders (148) and Prass et al. (147). In addition to bursts and spikes, train activity was further subdivided into A, B, and C trains (Figure 3) (154).

Spikes correspond to biphasic or triphasic potentials with 1 large peak (amplitude). Bursts are defined as an isolated complex of superimposed spikes arranged in a spindle-like fashion that shows several large peaks of up to 5,000 μV and lasts up to
several hundred milliseconds (Figure 2) (154). A-train is a unique sinusoidal waveform pattern with a typical high-frequency acoustic signal that always has a sudden onset, amplitude never exceeding 500 μV, a frequency of 60 to 200 Hz, and duration of milliseconds to several seconds (Figure 3). B-train is a regular or irregular sequence of a single spike or burst component (B – B spikes or B0 – B bursts) that has a gradual onset and a long duration from 500 ms to hours. C-train is characterized by a continuous EMG irregular activity (154).

Spikes and bursts occur immediately after direct mechanical trauma from surgical instruments near the CN and together with B- and C-trains are clinically irrelevant (133, 154). Nevertheless, the occurrence of A-trains is associated with FN injury (150, 151, 154). The A-train EMG pattern is highly suggestive of repetitive discharges that are found in chronic denervation processes and myopathies (154). These discharges are initiated by a spontaneously fibrillating muscle fiber that leads to the activation of several adjacent muscle fibers and the ephaptic reactivation of pacemaker fibers (154). Therefore, after nerve injury, the corresponding muscle fibers may become unstable and serve as a pacemaker because they are no longer under neural control (154). The first occurrence of A-trains can always be correlated with specific surgical maneuvers, especially the dissection of the tumor surface near the brainstem and intrameatal decompression (154).

Intraoperative Use. The main reason for using free-running EMG is to supply the surgical team with immediate information about nerve location and to give continuous feedback on any ongoing activity that could result in nerve injury (61, 63, 65, 159). Because of the apparent absence of delay, EMG activity after mechanical trauma may be valuable for localizing during tumor resection by warning the surgeon about nerve proximity even when the FN has not come into field (62, 88, 147, 148). Additionally, in the absence of neurotonic discharges, the surgery may proceed faster because the FN is expected to be far from the working area (62, 84, 174). Although only train activity may indicate nerve injury (147, 148, 150, 151, 154), any EMG activity may serve as a warning sign of FN manipulation, thereby allowing changes in the surgical strategy before irreversible injury has occurred (30, 40, 56, 154). As a result, surgical trauma and consequently the risk of FN damage are minimized when continuous feedback of the nerve’s functional status is made available (154).

Function Prediction. Although there is agreement regarding the usefulness of continuous EMG monitoring for detecting unexpected mechanical trauma (61, 63, 65, 159), its role in facial function prediction is still controversial (54, 56, 66, 88, 133, 134, 196). This may be partially due to the lack of standardization of EMG patterns in published studies and difficulty in the analysis and quantification of the intraoperative findings because of limited availability of the related software (133, 134, 149, 151, 154).

Table 2 provides a detailed analysis of the published studies regarding the function prediction of free-running EMG.

In previous studies, the intensity and frequency of train activities were found to be correlated with postoperative FN outcome (61, 62, 98, 133, 134). Because of this, the presence of high-frequency and high-amplitude trains (133) or even intensity reduction of the train activity during the final stages of tumor resection were indicative of poor postoperative outcome (98, 134). However, the detailed analysis of the EMG patterns indicates that the significance of the EMG potentials is not related to their amplitudes but to the waveform patterns (149, 151, 154). As mentioned earlier, only train activities are related to FN injury, especially A-trains (149, 151, 154).

Rømstøl et al. (154) identified this type of EMG activity in almost all of the patients affected by postoperative facial paresis. A sensitivity of 86% and a specificity of 89% were calculated, indicating that A-train occurrence was a highly accurate predictor of postoperative facial paresis (154). In that study, however, a correlation between the number of A-trains and postoperative facial function could not be demonstrated (154). Thereafter, Prell et al. (151) showed that a quantitative EMG parameter, namely the train time, was a reliable indicator of postoperative facial palsy. Interestingly, 2 time thresholds could be defined, 0.5 s and 10 s (151). For patients with normal preoperative function, a train time of <0.5 s is strongly correlated with a good postoperative outcome, whereas the 10-s time threshold is associated with facial deterioration in patients with normal preoperative function and those affected by preoperative facial palsy (151).

It is worth mentioning that both studies provided an offline analysis of the intraoperative findings so that waveforms were evaluated retrospectively after the end of the surgical procedure, comprising the major limitation of the technique. Recently, the study was continued by developing software capable of recognizing and quantifying A-trains in real time (149). The software shows train time activity continuously through monitor inlet in the surgeon view depicted as a traffic light display (green [< 0.125 s]; yellow [0.125-2.5 s]; red [2.5-10 s]; and black (> 10 s)) (149). Such threshold levels were compared with those obtained in the offline analysis, rendering lower amounts of time by a factor of 4, in which 0.5 s of offline analysis corresponded to 0.125 s of real-time analysis. For patients with normal preoperative facial function, train time activity lower than 0.125 s was strongly correlated with good postoperative outcome, whereas 2.5-s and 10-s thresholds mostly indicated good postoperative function and marked dysfunction, respectively (149). Conversely, for patients with preoperative facial dysfunction, only the 2.5-s threshold was defined indicating favorable or unfavorable facial function. The surgical strategy was modulated according to intraoperative findings in a way that subtotal or near-total resection was considered when the red and black thresholds were achieved. This situation occurred in 4 of 30 studied patients, whereas in the other 4 patients, threshold levels were exceeded, but the surgical procedure was continued because of the younger age (149). That study is unique due to first-time demonstration of real-time FN monitoring with interpretation independent from the electrophysiological team. It may contribute in the near future to increasing reliability of facial function prediction during surgical procedures.

In addition to train time, postoperative complete facial palsy may also be suggested in patients with silent EMG responses, in which no more bursts can be evoked at the end of tumor removal (98, 134). This may represent axonal damage because healthy axons are likely to respond to mechanical manipulation (63). The combination of continuous EMG monitoring and DES may improve the prediction of facial function
## Table 2. Summary of Published Studies on the Predictive Value of Continuous EMG Monitoring

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design</th>
<th>Number of Patients</th>
<th>Histology</th>
<th>Channels, Muscles</th>
<th>IOFNM Criteria</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harner et al., 1987 (62)</td>
<td>Retro</td>
<td>48</td>
<td>VS</td>
<td>1, 2 to 4 (oculi, oris, mentalis, masseter, or temporalis)</td>
<td>Intensity of neurotonic discharge</td>
<td>Severe neurotonic discharges were strongly correlated with postoperative facial dysfunction</td>
</tr>
<tr>
<td>Harner et al., 1988 (61)</td>
<td>Retro</td>
<td>91</td>
<td>VS</td>
<td>1, oculi or oris, mentalis, masseter, temporalis</td>
<td>Intensity of neurotonic discharge</td>
<td>Predicted the degree of postoperative facial weakness</td>
</tr>
<tr>
<td>Lenarz and Ernst, 1994 (98)</td>
<td>Retro</td>
<td>30</td>
<td>CPA</td>
<td>2, oculi, oris</td>
<td>1. Number of train events 2. Ratio (trains/h)</td>
<td>Correlated with the postoperative facial function (&gt;26 trains, HB III or greater); &gt;5.4 trains/h, predictive of poorer immediate postoperative function (HB III or greater)</td>
</tr>
<tr>
<td>Eisner et al., 1995 (40)</td>
<td>Retro</td>
<td>16</td>
<td>Brainstem</td>
<td>1, for both oculi, 1, for both oris</td>
<td>Duration of PSA 1. Slight PSA, EMG activity for a few seconds 2. Extreme PSA, EMG activity for several hours, similar to trains</td>
<td>Extreme PSA, permanent postoperative deficit; Any EMG activity, normal function; Constant EMG activity/slight PSA, transient or incomplete palsy</td>
</tr>
<tr>
<td>Grabb et al., 1997 (56)</td>
<td>Retro</td>
<td>17</td>
<td>Fourth ventricle</td>
<td>1, for both oculi, 1, for both oris</td>
<td>Facial muscle EMG activity</td>
<td>The presence of irritation activity was associated with postoperative facial weakness</td>
</tr>
<tr>
<td>Hone et al., 1997 (66)</td>
<td>Pros</td>
<td>27</td>
<td>VS</td>
<td>2, frontalis, oris</td>
<td>1. Number of spontaneous or mechanically induced contractions (&gt;20) 2. Number and length of trains with repetitive activity (&gt;199 s)</td>
<td>74% had more than 20 contractions and 59% had more than 200 s of train activity; Neither was predictive of postoperative FN function.</td>
</tr>
<tr>
<td>Kombos et al., 2000 (88)</td>
<td>Pros</td>
<td>60</td>
<td>CPA</td>
<td>2, oculi, oris</td>
<td>Duration of EMG activity 1. Single discharges or &lt;2 min 2. EMG activity of 2–5 min 3. EMG activity &gt;5 min 4. Loss of EMG activity</td>
<td>&lt; 2 min EMG activity, good immediate and long-term function; 2-5 min EMG activity, 60% good immediate function (93.3% sensitivity and PPV); &gt; 5 min EMG activity (73.3% sensitivity and PPV), 67% fair and 33% poor immediate function; Loss of EMG, all poor immediate and late function; Burst duration does not necessarily correlate with postoperative outcome</td>
</tr>
<tr>
<td>Romstöck et al., 2000 (154)</td>
<td>Pros</td>
<td>30</td>
<td>CPA</td>
<td>3, oculi, oris, nasalis</td>
<td>Analysis of EMG waveform patterns (spikes, bursts, trains)</td>
<td>Occurrence of A-trains is a reliable predictor of postop facial palsy; Spikes, bursts, B and C-trains were clinically irrelevant</td>
</tr>
<tr>
<td>Nakao et al., 2001 (133)</td>
<td>Pros</td>
<td>51</td>
<td>VS</td>
<td>2, oculi, oris; oris (motion detector)</td>
<td>Number, duration, frequency, and amplitude of train responses</td>
<td>Train duration (30 s to 20 min) and number (1 to 14) were not predictors of facial function; High-amplitude (≥ 250 μV), 85.7% HB V or VI at discharge; No trains, 77.8% facial palsy (HB VI) at discharge; High-frequency (bomber type), 80% HB V or VI at discharge.</td>
</tr>
<tr>
<td>Study</td>
<td>Study Design</td>
<td>Number of Patients</td>
<td>Histology</td>
<td>Channels, Muscles</td>
<td>IOFNM Criteria</td>
<td>Results</td>
</tr>
<tr>
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</tr>
<tr>
<td>Wedekind and Klug, 2001 (196)</td>
<td>Pros</td>
<td>33</td>
<td>CPA</td>
<td>2, oculi, oris</td>
<td>Analysis of EMG waveform patterns</td>
<td>The frequency of the first category was significantly higher in patients with good outcomes at immediate and at 3 mo (sens 69%, spec 94%). The frequency of the third category was higher but not significant in patients with poor postoperative outcome (immediate and long-term) (sens 45%, spec 89%). Continuous EMG recording does not provide reliable prediction of facial function</td>
</tr>
<tr>
<td>Nakao et al., 2002 (134)</td>
<td>Pros</td>
<td>49</td>
<td>VS</td>
<td>2, oculi, oris</td>
<td>Analysis of burst and train patterns</td>
<td>Irritable pattern, 91% HB III or better at discharge and 100% at 1 y; Silent pattern, 82% HB V or VI at discharge and HB III or better at 1 y; Stray pattern, all HB V or VI at discharge and HB III or better at 1 y; Ordinary pattern, 77% HB I/II at discharge and 92.3% HB III or better at 1 y.</td>
</tr>
<tr>
<td>Prell et al., 2007 (151)</td>
<td>Retro</td>
<td>40</td>
<td>VS</td>
<td>3, oculi, oris, nasalis</td>
<td>A-trains quantitative parameter (train time)</td>
<td>Reliable predictor of immediate and long-term FN outcome; Two thresholds, 0.5 s and 10 s; 0.5 s-threshold, train time less than threshold correlates with good postoperative function; 10 s-threshold, less than 10 s was correlated with less deterioration (1 HB grade) and more than 10 s (2 HB grades or more).</td>
</tr>
<tr>
<td>Prell et al., 2010 (149)</td>
<td>Pros</td>
<td>30</td>
<td>VS</td>
<td>3, oculi, oris, nasalis</td>
<td>Real-time A-trains (train time)</td>
<td>Reliable predictor of immediate and long-term outcome; Four thresholds, 0.125, 0.125 – 2.5, 2.5 – 10, and &gt;10 s; High correlation between train time and functional outcome so that greater train time indicates greater HB function or worse prognosis; 2.5 s, threshold that separates favorable from unfavorable (eye-endangering) outcomes.</td>
</tr>
</tbody>
</table>

Bipo, bipolar probe; CC, constant current; CMAP, compound muscle action potentials; CPA, cerebellopontine angle; CV, constant voltage; EMG, electromyographic; FN, facial nerve; HB, House and Brackmann classification; IAC, internal auditory canal; IOFNM, intraoperative facial nerve monitoring; Mono, monopolar probe; multi, multicenter study; Multich, multichannel; NA, not attributable; NPV, negative predictive value; Ot, otological procedures; PSA, pathological spontaneous activity; PPV, positive predictive value; Pros, prospective; Retro, retrospective; REZ, root exit zone; sens, sensitivity; spec, specificity; VS, vestibular schwannoma.
The Limitations of Standard Intraoperative FN Monitoring Techniques

Although there is an increasing rate of FN preservation due to the introduction of routine intraoperative FN monitoring (6, 135, 154, 159), facial weakness is still a complication of major concern in patients undergoing CPA surgery (6, 159). Triggered CMAP obtained with DES can only be used intermittently and after the identification of the nerve at the brainstem. This is particularly difficult in patients with large tumors, in whom the adequate placement of the stimulation probe is disturbed due to the anatomical distortion of the brainstem and late identification of the proximal FN that is inaccessible during most of the surgical procedure (6, 49, 154, 189). Thus, DES is highly dependent on the surgeons’ ability to locate correctly the exit zone of the FN on the brainstem (6). Some studies have demonstrated that proximal FN identification and the recording of the brainstem-to-distal IAC CMAP ratio cannot be performed in 30% to 35% of monitored patients owing to technical reasons, distorted anatomy, or surgical approach (6, 38). Intermittent use may also be cumbersome and may delay the surgical procedure because whenever stimulation is performed, a temporary stoppage in dissection is necessary (203). Therefore, DES may not afford a continuous assessment of the FN function even if this method is available in all cases (38).

Recently, Amano et al. (7) described a novel strategy for FN monitoring during VS resection, namely the continuous monitoring of evoked FN EMG, in which a specially designed electrode is applied at the REZ of the FN recording real-time EMG changes. Although the amplitude preservation ratio corresponded significantly to both immediate and late postoperative facial function (7), the dislocation rate of the electrode and the need for an adequate location of the FN REZ in large tumors comprise important limitations of the method. Conversely, this is possibly the first prototype, and the investigators should be strongly encouraged to go further in their research by creating new devices to improve continuous monitoring of evoked facial EMG and ultimately facial function after VS resection because it surpasses the intermittent use provided by DES.

Free-running EMG relies on neurotonic discharges in response to surgical maneuvers that can indicate injury to the FN (151, 154). A major limitation is that special software is necessary for either offline or real-time analysis. In addition, free-running EMG provides only an approximate correlation between the frequency of the neurotonic discharges and the degree of nerve injury so that neither their presence nor their absence assures the anatomical and functional integrity of the FN at the completion of tumor resection (63). Moreover, it is also worth noting that sharp transection of the FN may not evoke neurotonic discharges, whereas mechanical stimulation of the distal nerve stump that is still in continuity with the muscle may provoke EMG activities (63, 65, 76, 78). Both situations should be acknowledged because of their significant impact in function prediction when using free-running EMG.

Introduction of Motor Evoked Potential to FN Monitoring

Concurrently to the advances in EMG monitoring, Merton and Morton (119, 120) and Merton et al. (118) devised a protocol for obtaining muscle motor evoked potentials (MEP) of the upper and lower limbs through single-pulse electrical stimulation of the scalp in healthy subjects. Interestingly, a slight voluntary contraction of the contralateral target muscle (between 10% and 25% of the muscle strength) somehow focuses the stimulus in a way that the motor threshold is markedly reduced, a phenomenon called facilitation (118, 122). Spinal epidural recordings in humans have demonstrated that after single-pulse transcranial electrocortical stimulation (TES), 2 types of waves are conducted (18, 33). Direct depo-
Polarization of the motor cortex results in a large and brief wave, whose latency is compatible with the conduction time of the fast corticospinal tract fibers after vertical fiber depolarization without intervening synapses. This wave is called direct (D) wave (18, 33). After the D wave, several smaller waves are easily recorded, corresponding to horizontal fiber depolarization or transsynaptic activation of the motor cortex (18, 33). These waves are called indirect (I) waves (18, 33). After description, TES has been used in a wide variety of clinical and neurophysiological studies (122). One major problem is that it is relatively painful when used in awake subjects (18, 36, 102, 122).

Aside from TES, the human brain can also be stimulated by brief intense magnetic fields. In 1985, Barker et al. (12) described this noninvasive novel method of directly stimulating the motor cortex by using a pulsed magnetic field, in which less discomfort for the patients is produced over the electrical stimulation. The most obvious difference between electrical and magnetic stimulation of the brain is the pain perception in the scalp (18, 36, 102, 122). In addition, TES activates the corticospinal neurons, producing a direct stimulation of pyramidal outflow (D wave) followed by collateral activation (I waves), whereas magnetic stimulation activates the corticospinal tract indirectly by producing only I waves (18, 102). This explains the shorter latency of MEP after electrical stimulation (18, 122). For hand muscle MEP, the latency elicited by TES was 1.8 ms faster than that obtained with magnetic stimulation (122). Exception occurs, however, with the tilting of the magnetic coils that can induce the direct stimulation of the corticospinal tract and result in latencies comparable to those obtained after TES (18).

Because of the limitations of somatosensory evoked potential (SEP) and the “wake-up test” for ensuring motor pathway integrity, MEP was then applied to intraoperative monitoring of the motor function (34, 75, 102). Nonetheless, initially there was great difficulty in obtaining intraoperative muscle MEP because anesthetized patients are unable to facilitate MEP responses by voluntary contraction of the target muscles, as well as depression in cortical excitability owing to the use of many anesthetic agents (26, 75). Thus, further modifications of the MEP protocol were provided for recording under general anesthesia (75, 187). Taniguchi et al. (187) introduced a new protocol in which the MEP responses could be obtained without averaging, thereby providing real-time monitoring. Thereafter, the method of short trains of pulses was described, in which the MEP responses were enhanced after TES in anesthetized patients (75). TES intraoperative MEP monitoring is preferred to magnetic stimulation because the latter has particular disadvantages (106, 107, 109). Heating, which can be a problem if the coil is used for longer periods, especially when using the first constructed devices (18), and inaccurate positioning of the magnetic coil under the sterile drapes comprise the major disadvantages of intraoperative magnetic stimulation.

MEP has routinely been used to monitor major motor pathways intraoperatively during several neurosurgical procedures (33, 38, 102, 107, 156), especially during spinal surgeries (75, 89, 90, 96, 208, 209). The presence of muscle MEP indicates the preservation of the functional integrity of the motor cortex, the corticospinal tract, the alpha motor neurons, the peripheral nerve, and the neuromuscular junction (156).

Facial motor evoked potential (FMEP) obtained by TES of the contralateral face motor cortex recently has been introduced to monitor FN function and may be considered the most promising method in FN monitoring because it surpasses most of the disadvantages of standard techniques (4, 6, 38, 48, 49, 156, 189, 200, 210). FMEP interpretation is independent from the surgeon’s ability to locate the proximal FN at the brainstem and can facilitate recognition of waveform recordings obtained by free-running EMG (4, 38). For such reasons, Yingling and Gardi (203) have assigned the application of FMEP monitoring as the most significant advance in the field since the advent of EMG monitoring in the late 1970s.

The first reported use of FMEP was done by Zhou and Kelly in 2001 (210) during brain tumor resections in which only the orbicularis oris muscle was monitored. Despite the description of the first FMEP use, the predictive value of FMEP was not directly assessed in that study. The evoked responses on the facial channels were analyzed generally together with the limb MEP recordings, precluding definitive conclusions about their interpretation (210). Dong et al. (38) exclusively investigated the usefulness of orbicularis oris FMEP for prediction of postoperative facial function. successive studies have confirmed the value of adding FMEP monitoring to standard methods of IOFNM during skull base (6, 49) and CPA surgeries (4).

Although published FMEP protocols demonstrate similar stimulation parameters, rendering high rates of successful monitoring (4, 6, 38, 49), optimal configuration is yet to be defined, preventing widespread use of the technique. Technical refinements have improved the success rates of orbicularis oris FMEP monitoring contributing to better outcome prediction because both branches of the FN can be monitored throughout surgery (4, 49). A detailed discussion on FMEP protocols and parameters is provided elsewhere (4, 6, 38, 49).

Corticospinal tract injury, root or peripheral nerve trauma, stretching, ischemia, or pressure may all be responsible for pathologic MEP amplitude reductions (107). Several potentially confounding factors occur during CPA surgery, namely anesthesia, stimuli failure, scalp edema, and neuromuscular blockade (6, 210). Gradual muscle MEP amplitude fading could be a potential factor to justify false-positive results during stable anesthesia without scalp edema (105, 107). Such gradual evolution is an important differentiation of this phenomenon from a more abrupt pathologic MEP reduction (105, 108, 126). On the other hand, given that FMEP is generated by subpopulations of FN axons (38), false-negative results are supposed to be caused by minor injuries affecting axons not included in the FMEP that could ultimately lead to mild facial weakness without considerable FMEP changes (49).

Additionally, surgery in the semisitting position is susceptible to changes in MEPs and SEPs, which are not related to neurological impairment. These changes were presumably caused by the insulating effect of subdural air collection (6, 102, 107, 198, 210). Thus, we sought to investigate the correlation of MEP and SEP final-to-baseline amplitude ratios to the postoperative volumetry of frontoparietal subdural air collection in neurologically intact patients (2). Our results indicated that although SEP and MEP recordings may have limited interpretation during surgery in the semisitting position, it is not completely clarified why only a subgroup of patients operated on in the semisitting position develops such IOM changes. Moreover, although SEP amplitude reductions were associated with large subdural air collections, this was not ob-
served for the subset of patients with SEP attenuation and for the MEP monitoring, suggesting other pathophysiological mechanisms, such as brain shift, for the artificial amplitude reduction.

Intraoperative Use. TES is performed intermittently with brainstem auditory evoked potentials and SEPs by taking advantage of short intervals during changes of the surgical instruments or modifications of the microscope position by the surgeon. The surgical team should be always warned about the coming stimuli, especially during the microsurgical steps, due to undesirable movements as a consequence of transcranial stimulation. TES is accomplished using corkscrew-like electrodes inserted in the scalp and positioned at Cz and C3 or C4 (international 10-20 electroencephalography system) for left- or right-side stimulation, respectively. Stimulation is applied contralaterally to the affected side using 1, 3, or 5 rectangular pulses ranging from 200 to 600 V with 50 μs of pulse duration and an interstimulus interval of 2 ms. The number of pulses and stimuli intensity is increased according to facial and hand MEP responses. A train of 5 pulses is used only in cases of unsatisfactory response to a train of 3 pulses. Single pulse stimulation, longer latencies (>10 ms), and hand MEP recordings serve as control to ensure that the FN is not stimulated extracranially. Facial potentials are recorded from the same electrodes and muscle groups used for DES and free-running EMG (Figure 4) (4).

Function Prediction. An FMEP amplitude ratio reduction of 50% at the end of the surgery has been identified as a good predictor for postoperative FN outcome after CPA and skull base surgeries (4, 6, 38, 49). This criterion was arbitrarily defined by considering the wide variability of FMEP amplitude between patients (6); however, there is an obvious influence from the initial limb MEP studies, which were based on clinical experience with intraoperative SEP monitoring (208). Because of the unique cortical representations of limbs and face (or even superior and inferior levels of the face), we previously provided an active search for the best threshold levels with the assumption that MEP from both areas might have a different interpretation (4). Our hypothesis was proved correct so that 2 different thresholds of final-to-base FMEP ratios for orbicularis oculi and oris muscles were encountered: 80% and 35%, respectively (4). Considering the best results obtained in the monitoring of orbicularis oris muscle, we proposed that deterioration of FMEP ratios to between 80% and 35% should lead to alterations in the surgical strategy in order to avoid definitive motor injury (4). Further support of such management strategy is found for limb MEP, in which an amplitude reduction of more than 50% should be promptly reported to the surgical team for changing surgical maneuvers (90, 91, 126, 208-210). Table 3 provides a detailed analysis of the published studies regarding the function prediction of FMEP.

Although FMEP reduction is a good predictor of postoperative facial function (6, 38), only the initial and final FMEP amplitude values are considered for function prediction. We hypothesized that intraoperative variation of FMEP amplitude could also correlate with postoperative facial function, even if final-to-base amplitude ratios remain above the 50% threshold level. Hence, an event-to-base FMEP amplitude ratio might reach better results in predicting immediate and late postoperative facial function.

Additionally, as traditional MEPs, FMEPs represent CMAP recordings and may be evaluated according to quantitative EMG, which is currently applied for techniques involving a detailed analysis of CMAP characteristics such as amplitude, latency, complexity, duration, and area under the curve (143). Amplitude is by far the most-used quantitative parameter for intraoperative FMEP monitoring (4-6, 38, 48, 49).

Conversely, waveform morphology is an underestimated CMAP parameter for intraoperative MEP monitoring. In this regard, we have conducted a study to analyze intraoperative electrophysiological changes in FMEP waveform morphology and amplitude and their correlation to postoperative facial function during VS resection (3). Analysis of correlation coefficients revealed a significant statistical negative correlation with the immediate and late postoperative FN outcome, such that greater FMEP amplitude and complexity predicted better FN function during all surgical stages directly related to tumor manipulation, especially for orbicularis oris recordings.

Our findings justify modifications of the surgical strategy based on FMEP deterioration during tumor manipulation due to increased risk of FN injury. We therefore support event-to-base FMEP monitoring based on our results, which confirm previous findings showing that moving surgical maneuvers to different areas permits FN fibers to recover (6), as described for the cochlear nerve (51) and spinal cord (156). In addition, these results in facial function prediction indicate that waveform complexity seems to be independent of FMEP amplitude, serving as an intraoperative electrophysiological indicator of FN integrity.

What to Do when Intraoperative FN Electrophysiological Parameters Deteriorate? In addition to surgery stoppage, irrigation with warm saline, and the wait for recovery used for limb MEP deterioration (89, 126), patients affected by FN intraoperative electrophysiological deterioration may be en-
<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design</th>
<th>Number of Patients</th>
<th>Histology</th>
<th>Pulse (μs)</th>
<th>Stimulus Protocol (Trains/ ISI)</th>
<th>Intensity</th>
<th>Electrode Montage</th>
<th>Channels, Muscles</th>
<th>IOFNM criteria</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhou and Kelly, 2001 [210]</td>
<td>Pros</td>
<td>50</td>
<td>Brain tumor</td>
<td>500</td>
<td>5, frequency 0.5–2 Hz</td>
<td>40–160 mA</td>
<td>1–2 cm anterior to C3 and C4</td>
<td>1, oris</td>
<td>Persistent MEP decrease of &gt;50%</td>
<td>MEP amplitude reductions were associated with postoperative motor deficits. The degree of amplitude reduction was correlated with the degree of immediate postoperative worsening. No mention of facial function.</td>
</tr>
<tr>
<td>Dong et al., 2005 [38]</td>
<td>Pros</td>
<td>76</td>
<td>Skull base</td>
<td>50/500</td>
<td>3–4, ISI 1 or 2 ms</td>
<td>100–400 V</td>
<td>1 cm anterior to C3/C4 and CZ (M3/M4-MZ)</td>
<td>1, oris</td>
<td>Final-to-baseline MEP ratio</td>
<td>Significant immediate postoperative facial deficits predicted: 50% ratio, sens 100%, spec 88%; 35% ratio, sens 91%, spec 97%; 0% ratio (loss), sens 64%, spec 100%. FMEP loss accounted for all patients who developed complete facial palsy postoperatively.</td>
</tr>
<tr>
<td>Akagami et al., 2005 [6]</td>
<td>Pros</td>
<td>71</td>
<td>Skull base</td>
<td>50</td>
<td>3–5, ISI 1–3 ms</td>
<td>200–400 V</td>
<td>C3/C4 and CZ</td>
<td>1, oris</td>
<td>Final-to-baseline MEP ratio</td>
<td>A 50% final-to-baseline ratio predicted immediate HB I/II facial function.</td>
</tr>
<tr>
<td>Fukuda et al., 2008 [49]</td>
<td>Retro</td>
<td>26</td>
<td>Skull base</td>
<td>NA</td>
<td>5, ISI 1 ms</td>
<td>180–550 V</td>
<td>C3/C4 and CZ</td>
<td>2, oculi, oris</td>
<td>Final-to-baseline MEP ratio</td>
<td>A 50% threshold consistently predicted immediate HB I/II facial function and palsy of both muscles.</td>
</tr>
<tr>
<td>Acioly et al., 2010 [4]</td>
<td>Retro</td>
<td>60</td>
<td>CPA</td>
<td>50</td>
<td>3 or 5, ISI 2 ms</td>
<td>200–600 V</td>
<td>C3/C4 and CZ</td>
<td>2, oculi, oris</td>
<td>Final-to-baseline MEP ratio</td>
<td>Immediate postoperative facial function correlated significantly with the FMEP ratio in the orbicularis oculi muscle at 80% amplitude ratio and orbicularis oris muscle at 35% ratio; FMEP loss was always related to postoperative facial paresis.</td>
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### Table 3. Continued

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design</th>
<th>Number of Patients</th>
<th>Histology</th>
<th>Pulse (µs)</th>
<th>Stimulus Protocol (Trains/ ISI)</th>
<th>Intensity</th>
<th>Electrode Montage</th>
<th>Channels, Muscles</th>
<th>IOFNM criteria</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acioly et al., 2011 (3)</td>
<td>Retro</td>
<td>35</td>
<td>VS</td>
<td>50</td>
<td>3 or 5, ISI 2 ms</td>
<td>200–600 V</td>
<td>C3/C4 and CZ</td>
<td>2, oculi, oris</td>
<td></td>
<td>FMEP amplitude ratio and waveform complexity correlated significantly with the postoperative facial function at discharge and at the last follow-up only during the surgical stages related to tumor manipulation itself, namely TuDis, TuRes and final. Acute FMEP amplitude ratio deteriorations of &gt;50% in orbicularis oculi and oris corresponded to postoperative facial palsy in 85.7% and 60% of patients, respectively. Deterioration of the FMEP waveform complexity [either from biphasic to loss or from polyphasic to biphasic or loss] was observed in oculi in 7 patients and in oris in 5 patients. Facial paresis occurred in all patients in whom waveform deterioration was documented on oris FMEP. Waveform complexity seems to represent an additional, independent quantitative parameter that can be used for FMEP monitoring.</td>
</tr>
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</table>

**Bipo, bipolar probe; CC, constant current; CMAP, compound muscle action potentials; CPA, cerebellopontine angle; CV, constant voltage; EMG, electromyographic; FMEP, facial motor evoked potential; FN, facial nerve; HB, House and Brackmann classification; IAC, internal auditory canal; IOFNM, intraoperative facial nerve monitoring; ISI, interstimulus interval; MEP, motor evoked potential; Mono, monopolar probe; multich, multichannel; NA, not attributable; NPV, negative predictive value; Ot, otological procedures; PPV, positive predictive value; Pros, prospective; Retro, retrospective; REZ, root exit zone; sens, sensitivity; spec, specificity; VS, vestibular schwannoma.**
rolled in a vasoactive treatment (166, 183). It was initially proposed for hearing preservation in patients with increasing risk of delayed hearing loss after VS resection based on unstable intraoperative brainstem auditory evoked potentials (183).

The significant increase in hearing preservation observed motivated retrospective evaluation of the facial function in those patients (183). Patients were scheduled for topical and systemic treatment for 10 days. At the end of the surgery, a nimodipine-soaked gel foam paty was applied over the CN together with the infusion of intravenous nimodipine (15 to 30 µg/kg/h). At the first postoperative day, hydroxyethyl starch 6% (500 ml, twice per day) was added for hemodilution. The results were encouraging, especially for patients suffering from complete facial palsy (House-Brackmann VI), in whom 6.7% of the treated group maintained such clinical grades after 1-year follow-up, whereas in the untreated group, 62.5% had complete facial dysfunction (183).

The assumption was further investigated with a prospective and randomized design (166). Patients were stratified in either prophylactic or therapeutic groups according to intraoperative deterioration of FN monitoring (166). Prophylactic vasoactive treatment showed significantly better results in terms of CN preservation during VS resection (166). From these data, a randomized trial is reasonable and it is possible in a near future to implement vasoactive treatment routinely for VS surgeries.

CONCLUSIONS

Before the advent of FN intraoperative monitoring, facial palsy was an acceptable sequela of CPA surgeries, as stated by Dandy in 1925 (31). Since its description, more than a century ago, several technical refinements and the introduction of additional methods of FN monitoring have contributed to the significant advances achieved in terms of anatomical and functional preservation of the FN. Currently, standard monitoring techniques comprise DES, free-running EMG, and FMEP. Although there is general agreement in the satisfactory functional prediction of different electrophysiological criteria, the lack of standardization in electrode montage and stimulation parameters precludes a definite conclusion regarding the best method. Moreover, studies emphasizing comparison between criteria or even multimodal monitoring and its impact on FN anatomical and functional preservation are still lacking in the literature.

Because of the increasing introduction of new methods and electrophysiological criteria of function prediction, development of new software capable of recognizing and quantifying each criteria in real time would be very helpful for both surgeons and electrophysiologists in the prevention of permanent facial dysfunction. The future is promising because intraoperative FN monitoring is still an evolving technique comprising an interesting field of research.

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