

# Migraine Surgery: A Plastic Surgery Solution for Refractory Migraine Headache

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**Summary:** Migraine headache can be a debilitating condition that confers a substantial burden to the affected individual and to society. Despite significant advancements in the medical management of this challenging disorder, clinical data have revealed a proportion of patients who do not adequately respond to pharmacologic intervention and remain symptomatic. Recent insights into the pathogenesis of migraine headache argue against a central vasogenic cause and substantiate a peripheral mechanism involving compressed craniofacial nerves that contribute to the generation of migraine headache. Botulinum toxin injection is a relatively new treatment approach with demonstrated efficacy and supports a peripheral mechanism. Patients who fail optimal medical management and experience amelioration of headache pain after injection at specific anatomical locations can be considered for subsequent surgery to decompress the entrapped peripheral nerves. Migraine surgery is an exciting prospect for appropriately selected patients suffering from migraine headache and will continue to be a burgeoning field that is replete with investigative opportunities. (*Plast. Reconstr. Surg.* 127: 181, 2011.)

**M**igraine headache is a primary neurologic disorder that is characterized by recurrent and debilitating episodes of headache accompanied by a variety of symptoms including nausea, vomiting, photophobia, phonophobia, sensory auras, and even aphasia, hemiplegia, or vertigo.<sup>1-4</sup> Epidemiologic studies have shown that an estimated 35 million Americans suffer from migraine headache, with a prevalence of approximately 18 percent in women and 6 percent in men.<sup>5,6</sup> The economic consequences of migraine headache have been estimated to exceed \$13 billion per year and are primarily related to absenteeism and lost productivity.<sup>7</sup> Unfortunately, this disorder is not isolated to adults and is also common in the pediatric population, with a prevalence of 5 percent in young children and 10 percent in adolescents.<sup>8</sup> Although awareness of the considerable burden of this disorder is increasing, experts maintain that migraine headache remains underdiagnosed and undertreated.<sup>9</sup> Treatment

of migraine headache has largely focused on behavioral and pharmacologic interventions. The wide range of medications available for migraine headache prophylaxis and abortive treatment underscores the fact that the pathophysiology of migraine headache is still poorly understood. Although significant progress has been achieved in the area of migraine headache management, there exists a distinct population of patients who do not receive adequate benefit from current treatment strategies and are considered “refractory” to the standard of care.<sup>10</sup>

Recently, a series of publications have suggested that in certain patients migraine headache can be surgically treated by decompressing peripheral nerves that act as migraine triggers. The peripheral theory was first proposed by Guyuron et al.<sup>11</sup> after making the clinical observation that patients who underwent endoscopic brow lift with surgical dissection of the supraorbital and supratrochlear nerves reported alleviation of migraine symptoms. This report coincided with studies that demonstrated the efficacy of botulinum

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*Received for publication April 24, 2010; accepted June 23, 2010.*

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DOI: 10.1097/PRS.0b013e3181f95a01

**Disclosure:** The authors declare that they had no financial interests or commercial associations during the course of this study. This article did not require any sources of funding.

toxin injection for the treatment of migraine,<sup>12,13</sup> which further substantiated the notion that peripheral mechanisms are important in the generation of migraine headache. However, some authors have argued against this theory and point to decades of scientific investigation in the field of neurology that emphasize a central mechanism for migraine headache. In this article, we provide an overview of the contemporary medical practices used for the treatment of this disorder, explore the limitations of these approaches, and discuss the growing evidence that supports the selected use of surgical techniques in the management of migraine headache.

### **PATHOGENESIS OF MIGRAINE HEADACHE**

Migraine headache was once thought to be a primary disorder of the cerebral vasculature, and acute attacks were attributed to episodes of intracranial vasodilation. However, recent literature suggests that vasodilation is likely an epiphenomenon rather than the cause of migraine headache.<sup>14</sup> It has been shown that periods of increased cerebral blood flow do not correlate temporally with the experience of migraine headache pain.<sup>15</sup> Imaging studies have demonstrated no sustained vascular changes when migraine episodes are induced by drugs such as sildenafil<sup>16</sup> or nitroglycerin.<sup>17</sup> In addition, intravenous infusion of vasoactive intestinal peptide, a known intracranial vasodilator, does not evoke migraine attacks.<sup>18</sup> Furthermore, analysis of the pharmacology of ergot alkaloid medications used to treat migraine headache revealed that these drugs also have the ability to affect neuronal transmission, which suggests that their efficacy could be unrelated to their vasoconstrictor properties and argues against a vascular cause of migraine.<sup>19</sup> These findings have led to the contemporary view of migraine headache as a primary neurogenic disorder.

Investigation into the pathogenesis of migraine headache has yielded several theories that attempt to explain the mechanisms of the disorder.<sup>20–22</sup> Research has attributed migraine genesis to hyperexcitability of occipital cortical neurons,<sup>23</sup> dysfunctional central brainstem structures,<sup>24</sup> and cortical spreading depression, a slowly advancing wave of diminished brain activity that is believed to produce auras.<sup>25</sup> There is also evidence that sensitization of the trigeminal nerve at the central and peripheral levels results in migraine generation.<sup>26</sup> Sensitization of primary afferent neurons of the trigeminal nerve has been shown to cause release of proin-

flammatory neuropeptides that produce a localized sterile meningitis and likely plays a pivotal role in the development of migraine headache pain.<sup>27–29</sup> Although the exact cause of neuropeptide release from sensitized trigeminal nerves remains unclear, the evidence supports a peripheral contribution to the initiation of migraine headache and suggests that mitigation of inciting peripheral nerve irritation may be beneficial in migraine headache prevention.

### **INADEQUATE EFFICACY OF PHARMACOLOGIC THERAPY**

Although pharmacologic intervention remains the primary modality of migraine headache treatment, its limitations must be explored to understand the necessity for alternative options, such as surgical intervention. Pharmacologic therapies are divided into preventive and abortive medications. Preventive drugs are considered if patients experience frequent migraine headaches that cause significant disability and regularly require the use of abortive drugs.<sup>30</sup> Although numerous drug classes have been used to prevent migraine attacks,<sup>31–33</sup> the mechanisms of action of these medications are unclear and their efficacy remains controversial. For example,  $\beta$ -blockers are most commonly prescribed for prophylaxis,<sup>34,35</sup> but some studies report only 30 to 40 percent improvement in migraine headache symptoms.<sup>36–39</sup> Other commonly used preventive medications include calcium channel blockers, antiepileptics, and antidepressants.<sup>40</sup> These drugs also demonstrate modest efficacy, with success rates from clinical trials generally less than 50 percent.<sup>41,42</sup> Furthermore, these medications often have side-effect profiles that may preclude many patients from initiating or continuing treatment.<sup>43</sup>

Abortive medications are used to terminate an acute migraine episode. The ergot alkaloids (e.g., ergotamine) were used as the first migraine-specific medications because of their strong  $\alpha$ -adrenergic agonist activity and subsequent vasoconstriction.<sup>19</sup> However, use of these drugs largely declined as a result of undesirable side effects with chronic treatment, including cerebral, myocardial, and peripheral ischemia; hypertension; and cardiac arrhythmias.<sup>44</sup> Aspirin and other nonsteroidal antiinflammatory drugs are now considered first-line treatment for most patients with migraine headache because of their over-the-counter availability and modest efficacy in clinical trials.<sup>45</sup> Antiemetics such as metoclopramide are also recommended for acute migraine headache and have the added benefits of

treating associated nausea and vomiting.<sup>40</sup> When these drugs fail to abort migraine attacks, triptan medications (e.g., sumatriptan) are used as backup agents and are often initial therapies for patients with severe migraine headache.<sup>46</sup> Triptans act as selective serotonin agonists at various 5-hydroxytryptamine 1 receptors and produce preferential cerebral vasoconstriction along with decreased trigeminal nerve-mediated vasodilation and dampening of central pain transmission at the trigeminal nucleus.<sup>40</sup> Although common side effects such as flushing, tingling, and chest tightness are well tolerated in select patients,<sup>47</sup> severe cardiac and neurologic reactions have been reported, and these drugs should be avoided in patients with a history of ischemic cardiac, cerebrovascular, or peripheral vascular disease.<sup>44</sup> Recent data have challenged the reputation of the triptan medications as the standard therapy. Ferrari et al.<sup>48</sup> performed a meta-analysis of 53 controlled clinical trials involving 24,089 patients to facilitate evidence-based guidelines for the available triptan drugs (Table 1). These data reveal that the triptans achieve a relatively modest pain-free response rate and show a substantial rate of recurrence. The superiority of triptan medications has also been questioned by other authors who demonstrated similar migraine abortive efficacy when comparing triptan and nonsteroidal antiinflammatory drug treatment regimens.<sup>49,50</sup>

**Table 1. Efficacy of Available Triptan Medications\***

	Pain-Free at 2 hr		Sustained Pain-Free Rate†	
	%	95% CI	%	95% CI
Sumatriptan				
25 mg	23.4	21.0–25.9	16.7	14.5–18.9
50 mg	28.7	26.5–30.9	19.8	17.8–21.8
100 mg	28.9	27.2–30.5	20.0	18.2–21.3
Zolmitriptan				
2.5 mg	29.1	26.6–31.7	19.0	16.1–21.8
5 mg	32.4	29.7–35.1	21.9	19.3–24.6
Naratriptan, 2.5 mg	22.4	20.0–24.7	15.9	13.4–18.5
Rizatriptan				
5 mg	30.5	28.4–32.5	18.9	17.0–27.3
10 mg	40.1	39.3–42.0	25.3	23.7–26.9
Eletriptan				
20 mg	16.4	13.2–19.7	10.6	7.7–13.5
40 mg	27.2	25.2–29.2	20.9	19.1–22.7
80 mg	33.0	30.5–35.4	25.0	22.8–27.2

CI, confidence interval.

\*Data from Ferrari MD, Roon KI, Lipton RB, Goadsby PJ. Oral triptans (serotonin, 5-HT<sub>1B/1D</sub> agonists) in acute migraine treatment: A meta-analysis of 53 trials. *Lancet* 2001;358:1668–1675.

†Proportion of patients who were pain-free at 2 hours following administration dose and did not have recurrence of moderate or severe headache requiring rescue medication for at least 24 hours.

In summary, the evidence suggests that although a certain population of migraine patients may benefit from the available preventive and abortive medications, there remains a large subset of sufferers who will continue to experience debilitating migraine headaches and are therefore refractory to current medical management. Furthermore, the adverse events and contraindications of many of the existing pharmacologic options will preclude some patients from using these drugs. Those patients who fail or demonstrate intolerance to conservative treatment and remain symptomatic should be considered for possible surgical management.

### BOTULINUM TOXIN: SUPPORT FOR A PERIPHERAL MECHANISM

Recently, botulinum toxin has been used as a new approach to treat patients whose migraine headaches are not alleviated by current drug therapy. Botulinum toxin acts to block the presynaptic release of the neurotransmitter acetylcholine from neuromuscular and parasympathetic junctions, making it an effective treatment for a variety of spastic disorders such as blepharospasm, strabismus, and dystonia, and autonomic conditions such as hyperhidrosis.<sup>51,52</sup> The chemodenervation produced by botulinum toxin is reversible and generally lasts from 3 to 6 months.<sup>53</sup> The proposed mechanism of action of botulinum toxin in migraine prophylaxis relates to the reduction or elimination of migraine triggers that consist of peripheral nerves that are sensitized because of external compressive forces from surrounding anatomical structures. Although botulinum toxin can directly prevent this sensitization by inhibiting release of inflammatory neuropeptides,<sup>29</sup> its efficacy in migraine headache is likely attributable to reduction of peripheral nerve irritation resulting from compression by craniofacial muscle contraction. This theory is supported by experience with patients who have a nasal septal migraine trigger, which involves contact between a deviated septum and an enlarged turbinate that compresses the mucosal branches of the trigeminal nerve and does not respond to chemodenervation of other migraine trigger sites by means of botulinum toxin. Surgical deactivation of this trigger site is effective in select patients and confirms the important role of external compression as the primary cause of peripheral nerve sensitization.<sup>54–56</sup>

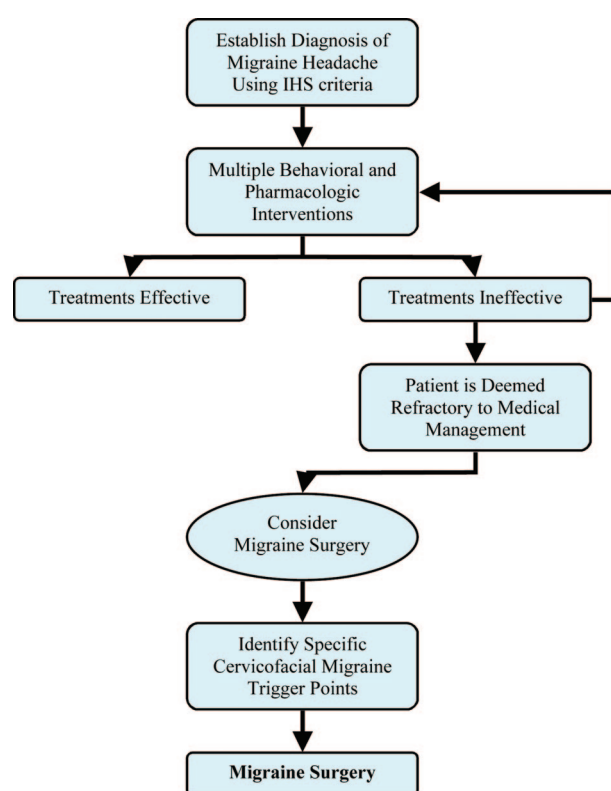
A number of studies have investigated the efficacy of botulinum toxin injection for treatment of migraine headache. Some clinical reports have displayed impressive response rates of up to 85

percent but were often limited by small treatment sizes and uncontrolled study designs.<sup>12,57–59</sup> Other double-blind, randomized, placebo-controlled studies have also corroborated a significant decrease in migraine headache symptoms compared with placebo after injection of botulinum toxin into various craniofacial muscles.<sup>13,60</sup> Dodick et al.<sup>61</sup> sought to eliminate the confounding variable of prophylactic medication use and performed a well-designed analysis of 172 migraine headache patients who were not taking preventive medications and confirmed that botulinum toxin injection significantly decreased headache frequency and severity compared with placebo and also decreased the use of abortive medications. Although it should be noted that other clinical trials have failed to demonstrate significant efficacy,<sup>62–64</sup> there remains persuasive evidence that botulinum toxin injection may be an effective preventive adjunct for a subset of migraine sufferers.

Although botulinum toxin injection has an emerging role in the management of migraine headache, its effects are temporary and its use is not without risks. Side effects may include blepharoptosis, diplopia, injection-site pain, and significant atrophy of the injected muscles, most notably seen in the temporalis muscles (temporal concavity known as hourglass deformity).<sup>65,66</sup> Therefore, botulinum toxin injection in this setting may best be used as a screening test for peripheral nerve irritation caused by muscle compression as a cause of migraine headache rather than a routine treatment modality. Those patients who are responders to botulinum toxin injection may then benefit from more definitive decompression of craniofacial peripheral nerves by surgical techniques.

### MIGRAINE SURGERY: PATIENT SELECTION AND PRACTICE

Surgery for migraine headache offers a novel treatment for patients who do not sufficiently respond to conventional therapies or tolerate the side effects of medications. For certain patients with migraine headache that is refractory to medical management, surgical intervention represents an effective alternative. The details of specific surgical techniques and craniofacial anatomy relevant to migraine surgery have been published<sup>67–73</sup>; however, an overview of this practice is summarized in this report (Fig. 1). Rigorous patient selection is paramount to successful migraine surgery. Researchers have readily used the expertise of board-certified neurologists and the diagnostic criteria set forth by the International Headache Society to screen for pa-



**Fig. 1.** Practice of migraine surgery for patients with refractory migraine headache. *IHS*, International Headache Society.

tients with true migraine headache, as many patients can have overlapping headache diagnoses, including tension-type headache, cluster headache, or cervicogenic headache.<sup>74</sup>

Once the diagnosis of migraine headache is made, a variety of validated questionnaires are used to collect baseline data regarding the characteristics of each patient's migraine headaches. The Migraine Disability Assessment Questionnaire is the most commonly used instrument of disability in headache studies and measures lost productivity in work and social activities.<sup>75</sup> Another widely used health survey is the Short Form-36 questionnaire, a generic instrument that, although not specific to migraine, has been shown to reliably detect outcomes in migraine patients undergoing therapy.<sup>76</sup> Quality of life in migraine patients can be assessed by using the Migraine-Specific Quality of Life instrument.<sup>77</sup> A more arbitrary but frequently used parameter is the migraine headache index, which is derived from multiplying the migraine frequency (days per month) by the intensity (zero to 10) and duration (fraction of 24 hours).

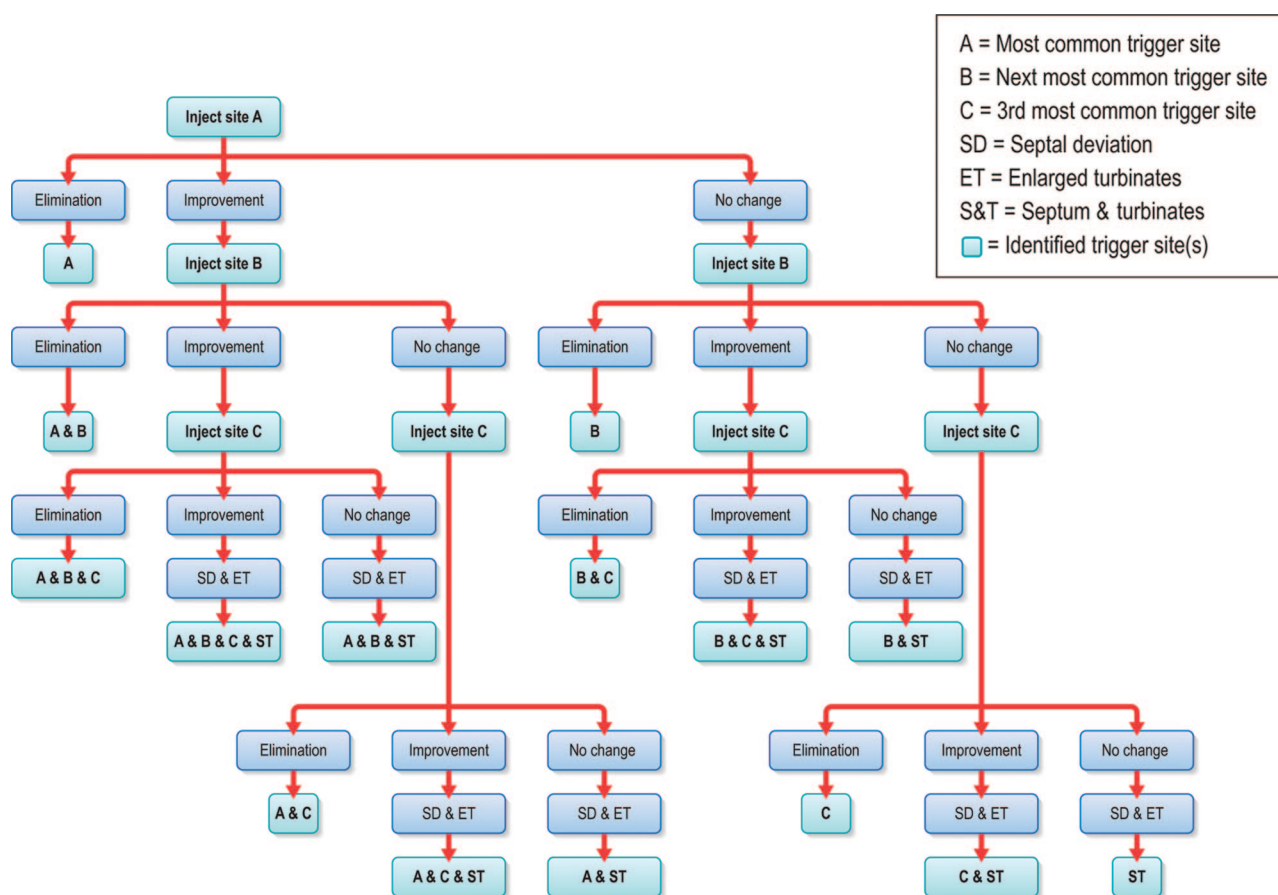
Appropriately selected patients then undergo a botulinum toxin trial injection in various de-



scribed trigger sites to determine whether they may benefit from surgical intervention. Alternatively, the inciting nerves can be directly neutralized using local anesthetic nerve blocks. Patients with migraine headache often describe pain originating from the forehead, temple, or occiput, and these locations consistently correlate with specific migraine triggers. The frontal, temporal, and occipital triggers involve peripheral nerves that can be compressed by craniofacial muscles. The nasal septal trigger is often associated with retroocular pain and is readily discovered by intranasal examination. An algorithm for identifying migraine triggers by means of sequential botulinum toxin injection (Fig. 2) has been published.<sup>67</sup> If intervention with botulinum toxin yields a sustained elimination of migraines or significant improvement, defined as at least 50 percent reduction from baseline intensity and/or frequency for at least 4 consecutive weeks, surgical management should be considered for each known trigger. This time course may not be feasible for out-of-town

patients; however, reliable detection of migraine triggers can still be achieved by using local nerve blocks, a single-stage injection of botulinum toxin into the predominate trigger site, or computed tomographic confirmation of septal deviation with turbinate enlargement.

Patients with frontal migraines may undergo resection of the glabellar muscle group, including the corrugator supercilii, depressor supercilii, and procerus muscles, using a palpebral incision to access the supraorbital and supratrochlear nerves, which are often compressed within the substance of these muscles. Temporal migraines can be treated with endoscopic avulsion of the zygomaticotemporal branch of the trigeminal nerve as it passes through the body of the temporalis muscle. If both triggers are involved, the glabellar muscle resection is also performed endoscopically. For migraines originating from the occipital region, the greater occipital nerve may be decompressed from its course through the semispinalis capitis muscle. Finally, a nasal septal trigger can



**Fig. 2.** Identification of migraine trigger sites by botulinum toxin injection. (From Guyuron B, Becker D. Surgical management of migraine headaches. In: Guyuron B, Eriksson E, Persing JA, eds. *Plastic Surgery: Indications and Practice*. Philadelphia: Elsevier; 2009: 1658. Used with permission.)

be eliminated by performing septoplasty with turbinectomies to cease contact between these structures. This technique has been reviewed by Behin et al.,<sup>54,78</sup> who propose that irritation of peripheral trigeminal afferents between intranasal structures causes release of neuropeptides, which lowers the threshold for migraine headache initiation and facilitates refractoriness to conventional therapies.

### A REVIEW OF CLINICAL EVIDENCE

Several studies have investigated the potential for migraine surgery (Table 2).<sup>11,56,78–82</sup> The concept was first proposed by Guyuron et al.<sup>11</sup> in 2000, who showed in a retrospective report that 80 percent of 39 patients described elimination or improvement in their migraine headaches after undergoing corrugator supercilii muscle resection as part of forehead rejuvenation surgery. A successive prospective study substantiated this finding and reported a 95 percent rate of either complete alleviation or improvement in migraine headache with a mean follow-up of 347 days.<sup>79</sup> After recognition of the occipital and nasal septal trigger points as additional peripheral triggers of migraine headache, Guyuron et al.<sup>56</sup> presented another prospective study involving 89 patients who were diagnosed with peripheral migraine triggers by botulinum toxin injection and underwent surgical treatment. Results from this study showed that 92 percent of the treatment group experienced either complete elimination or significant improvement of symptoms after 1-year follow-up. In comparison, 16 percent of control patients reported migraine improvement and no control patients reported complete elimination. These interesting findings were corroborated by Poggi et al.<sup>81</sup> in a small retrospective study and Dirnberger and Becker<sup>80</sup> in a prospective study, who noted that surgery was less effective for patients with more severe migraine headache and that in these patients headaches were more likely to recur 4 to 6 weeks postoperatively.

Although these studies validated a peripheral mechanism for migraine headache, they were often limited by retrospective design and lacked control groups. Furthermore, criticism pointed to the placebo effect, which is a well-known entity in migraine headache research.<sup>83</sup> Multiple studies of various medical interventions for migraine headache have shown a response rate of up to 50 percent with placebo,<sup>84</sup> although no studies have previously reported a placebo effect attributable to surgical intervention. In 2009, Guyuron et al.<sup>82</sup> published a randomized, placebo-controlled trial that involved the surgical deactivation of frontal, temporal, and occipital trigger sites. After a single predominant trigger point was identified using botulinum toxin injection, patients were then assigned randomly to receive treatment surgery or sham surgery, which involved exposure of the anatomical triggers without decompression. In the treatment group, 84 percent reported significant improvement at 12 months compared with 58 percent in the sham group. More specifically, 57 percent of the treatment group experienced complete elimination of migraine headache compared with 4 percent in the sham surgery group (one of 26 patients). The authors noted that because only the principal trigger site was addressed for each treatment group, other potential triggers may have been untreated, which suggests that even higher response rates to surgery may have been attained if multiple sites had been addressed. The relatively high rate of symptomatic improvement in the sham surgery group was attributed to possible altered nerve function caused by surgical manipulation and the placebo effect.

These findings affirm the promise of surgical treatment of migraine headache in patients who are refractory to medical management and also provide the groundwork for additional scientific investigation in the field of migraine surgery. Future research will elucidate the anatomical relationships of migraine trigger points and possibly identify additional sites that have the capacity to

**Table 2. Summary of Migraine Surgery Studies**

Reference	Type of Study	Level of Evidence	No. of Patients	Response Rate (%)
Guyuron et al., 2000 <sup>11</sup>	Retrospective	III	39	80
Guyuron et al., 2002 <sup>79</sup>	Prospective	II	22	95
Dirnberger and Becker, 2004 <sup>80</sup>	Prospective	II	60	68
Guyuron et al., 2005 <sup>56</sup>	Prospective	II	89	92
Poggi et al., 2008 <sup>81</sup>	Retrospective	III	18	67
Guyuron et al., 2009 <sup>82</sup>	RCT	I	49	84
Guyuron, 2010*	Prospective	II	69	88

RCT, randomized controlled trial.

\*Submitted for review.

generate migraine headache. Furthermore, specific patient populations can be examined to compare the efficacy of surgical treatment. Research is currently being conducted to examine the long-term benefits of migraine surgery. Guyuron et al.<sup>85</sup> have completed a 5-year follow-up study that shows sustained improvement of migraine frequency, intensity, and duration in 61 of 69 subjects (88 percent). Another ongoing study is investigating the medicoeconomic value of migraine surgery and demonstrates a median total cost reduction of \$3950 at 5 years postoperatively, indicating that surgical intervention can lead to significant cost savings by obviating expenses associated with medications, doctor visits, and other financial burdens relating to migraine headache.<sup>86</sup> With confirmation of the efficacy of surgical deactivation of migraine trigger sites, we anticipate that the practice of migraine surgery will evolve and play an important role in the treatment of patients with migraine headache who do not tolerate or do not wish to continue medical interventions.

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