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Multiple Subpial Transections for Medically Refractory Epilepsy: A Disaggregated Review of Patient-Level Data

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BACKGROUND: Multiple subpial transections (MST) are a treatment for seizure foci in nonresectable eloquent areas.
OBJECTIVE: To systematically review patient-level data regarding MST.
METHODS: Studies describing patient-level data for MST procedures were extracted from the Medline and PubMed databases, yielding a synthetic cohort of 212 patients from 34 studies. Data regarding seizure outcome, patient demographics, seizure type, surgery type, and complications were extracted and analyzed.
RESULTS: Seizure freedom was achieved in 55.2% of patients undergoing MST combined with resection, and 23.9% of patients undergoing MST alone. Significant predictors for seizure freedom were a temporal lobe focus (odds ratio 4.9; 95% confidence interval 1.71, 14.3) and resection of portions of the focus, when feasible (odds ratio 3.88; 95% confidence interval 2.02, 7.45). Complications were frequent, with transient mono- or hemiparesis affecting 19.8% of patients, transient dysphasia 12.3%, and permanent paresis or dysphasia in 6.6% and 1.9% of patients, respectively.
CONCLUSION: MST is an effective treatment for refractory epilepsy in eloquent cortex, with greater chances of seizure freedom when portions of the focus are resected in tandem with MST. The reported rates of seizure freedom with MST are higher than those of existing neuromodulatory therapies, such as vagus nerve stimulation, deep brain stimulation, and responsive neurostimulation, though these latter therapies are supported by randomized-controlled trials, while MST is not. The reported complication rate of MST is higher than that of resection and neuromodulatory therapies. MST remains a viable option for the treatment of eloquent foci, provided a careful risk-benefit analysis is conducted.

KEY WORDS: Refractory epilepsy, Seizures, Eloquent, Palliative, Extratemporal lobe epilepsy

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Epilepsy becomes refractory in roughly one-third of newly diagnosed patients.[1] Surgical resection is an option for some of these patients, but is problematic when the seizure focus resides in eloquent cortex (such as language, motor, or visual areas).[2] For these patients, nondestructive neuromodulatory operations, such as vagus nerve stimulation (VNS), deep brain stimulation (DBS), and responsive neurostimulation (RNS), are alternative therapies that have generated increasing interest in the past decade.[3] Yet, one of the original techniques for treating eloquent seizure foci is sometimes overlooked: multiple subpial transections (MST).

ABBREVIATIONS: CI, confidence interval; **DBS,** deep brain stimulation; **MST,** multiple subpial transections; **OR,** odds ratio; **RNS,** responsive neurostimulation; **VNS,** vagus nerve stimulation

MST were first described by Frank Morrell and colleagues in 1989[4] as a means of treating refractory epilepsy when the focus lay in what they termed unresectable cortex.[4] The technique uses a small metal wire with a right-angle hook at its end, extending ∼4 mm. This hook is inserted into 1 side of a cortical gyrus, as close to the sulcus as possible, and then driven to the far side subcortically, toward the next sulcus. The bent end of the wire is subsequently raised to the pial surface, and the hook dragged under the

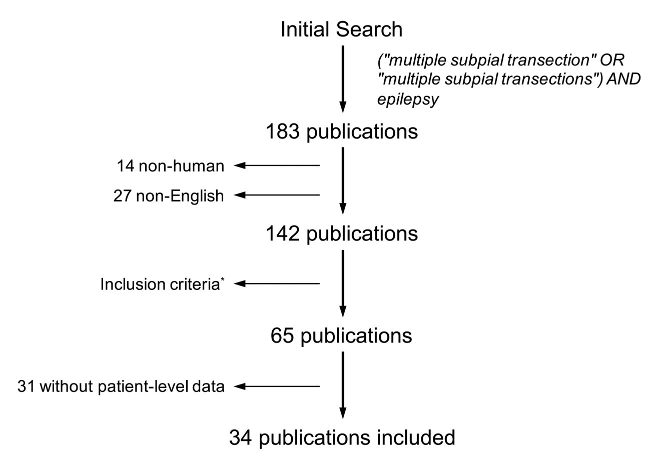

FIGURE 1. *Search results. All abstracts were reviewed and those not directly pertaining to MST were excluded. Further, articles were excluded when the results of MST could not be separated from the results of other interventions.*

pia back to the wire's entry point. This maneuver severs intracortical fibers along the wire's course, but spares subcortical white matter and U-fibers. Cuts are made perpendicular to the gyrus, from one sulcus to the other, and repeated roughly every 5 mm. The extent of the cuts spans the unresectable epileptic focus. The concept behind this technique is to prevent ictal activity from spreading throughout the focus via intracortial connections, but preserve the major subcortical inputs and outputs of the eloquent region. In their initial study of 20 patients, Morrell et al[4] reported a seizure freedom rate (Engel class I) of 55% with no significant induced deficits.

Motivated by these good outcomes, more than 100 studies of MST followed, all showing various rates of success. Yet, despite this large literature base, no systematic review of this technique was ever conducted to summarize the published data, or provide more general estimates of the technique's efficacy and rate of complications. While Spencer et al[5] produced an informative meta-analysis in 2002, their study compiled mostly unpublished data from 6 high-volume surgical centers.[5] It is unknown whether the select results from those few high-volume centers generalize to the wider neurosurgical community, as represented in the myriad articles published on MST before and after the Spencer meta-analysis. The upshot is that there remains no comprehensive literature review of all the work published on MST, which is the motivation of our work herein.

METHODS

The Medline and PubMed databases were queried on 6/13/2016 with the following Boolean search terms: ("multiple subpial transection" OR "multiple subpial transections") AND epilepsy. Nonhuman animal studies were excluded, and results were limited to English language publications (Figure 1). No time limits were placed on the searches. All abstracts were reviewed independently by 2 authors (JDR and HD) and those not directly pertaining to MST were excluded. Further, articles were excluded when the results of MST could not be separated from the results of other interventions. Only publications with patient-level reporting were included. References were analyzed of all relevant articles to find additional articles on MST. Individual data for each patient were extracted and combined, including patient age, gender, seizure semiology, surgical procedure, complications, outcome, follow-up, and epileptic focus location (Excel, Microsoft Inc, Redmond, Washington). Outcomes were divided into Engel class I vs Engel class IIto IV, since seizure freedom (class I) is the most common predictor of epilepsy surgery satisfaction.[6,7] Duplicate reports of the same patient were avoided by screening for patients with identical ages at surgery, genders, semiologies, procedure types, and epileptic focus location.

Statistical analysis was performed with SPSS Statistics version 23 (IBM Corp, Armonk, New York) and Matlab r2015a (Mathworks, Natick, Massachusetts). Summary statistics are presented with mean ± standard deviation. Numeric data were compared with Student's *t*-test, and categorical data with Pearson's χ^2 statistic. For multivariate analysis, logistic regression with backward conditional removal using a 0.10 cutoff was used for a maximum of 200 iterations.

RESULTS

One hundred thirty-nine articles concerning MST were identified through the Medline and Pubmed databases. After excluding irrelevant articles and articles with insufficient classification of results, 34 articles remained that described individual patient outcomes and characteristics (Figure 1).[8-41]

After disaggregating patient-level data from these studies, a synthetic cohort of 212 patients undergoing MST with or without adjunctive surgery was generated (Table 1). The mean age was 20.9 ± 13.7 yr and 36.9% were female; 54.4% had left-sided surgery, 42.4% had right-sided surgery, and 2.4% had bilateral surgery. Of these patients, only 47 (18.7%) had isolated MST without a concomitant surgery (eg, amygdalohippocampectomy, lesionectomy, corpus callosotomy, or VNS). Mean follow-up was 33.0 ± 20.0 mo.

Overall, 96 patients (45.3%) who underwent MST achieved seizure freedom (Engel class I). However, when MST was performed alone, without an adjunctive surgery (such as resection), only 16 of 68 patients (23.9%) were seizure-free (Figure 2). This is compared to 80 of 146 patients (55.2%) that achieved seizure freedom when MST was combined with resection or another procedure, such as callosotomy (Figure 1). When examining patient-level data, 2 significant predictors of seizure freedom (Engel class I) were found: (1) including a resection along with the MST (odds ratio [OR] 3.88; 95% confidence interval [CI] 2.02, 7.45), and (2) a seizure focus within the temporal lobe (OR 4.9; 95% CI 1.71, 14.3; Table 2).

Data describing seizure semiology were available for 167 patients (78.8%; Table 3). The most prevalent seizures were complex partial (59.7%), followed by simple partial (14.7%). The seizure types associated with the best outcomes were epilepsia partialis continua (66.7% Engel class I), syndromic epilepsies

TABLE 1. Studies Evaluating MST with Patient-Level Data

Study	Year	# Patients	Mean age	Mean follow-up	# Seizure free (%)
Devinsky et al[8]	1994	3	39.7 ± 10.2	12.7 ± 0.6	2 (67)
Wyler et al[9]	1995	6	23.2 ± 11.5	14.3 ± 3.9	1 (16.7)
Rougier et al[10]	1996	7	26.0 ± 10.7	21.4 ± 15.4	1 (14.3)
Patil et al[11]	1997	27	22.2 ± 15.4	26.9 ± 11.7	11 (40.7)
Hufnagel et al[12]	1997	22	23.0 ± 11.8	18.1 ± 6.9	9 (40.1)
Oguni et al[13]	1998	1	15	25	1 (100)
Molyneux et al[14]	1998	1	19	9	1 (100)
Asano et al[15]	1999	1	14	36	1 (100)
Akimura et al[16]	2000	1	25	22	1 (100)
Arita et al[17]	2000	1	17	30	1 (100)
Schramm et al[18]	2001	1	39	7	0
Mittal et al[19]	2001	1	8	21	1 (100)
Irwin et al[20]	2001	5	7.9 ± 2.3	53.8 ± 20.6	5 (100)
Ma et al[21]	2001	1	22	2	1 (100)
Cheng et al[22]	2001	1	14	16	1 (100)
Shimizu et al[23]	2001	1	12	24	0
D'Giano et al[24]	2001	1	6	12	1 (100)
Otsubo et al[25]	2001	7	12.1 ± 3.9	30[a]	3 (42.9)
Bernasconi et al[27]	2001	2	22.5 ± 16.3	48.0 ± 50.9	1 (50.0)
Otsubo et al[26]	2001	3	10.0 ± 3.6	33.3 ± 1.2	3 (100)
Schramm et al[28]	2002	21	25.6 ± 10.1	48.2 ± 18.5	1 (4.8)
Romanelli et al[29]	2002	1	10	26	1 (100)
Onal et al[30]	2003	30	11.1 ± 4.5	32.4 ± 12.2	11 (36.7)
Devinsky et al[31]	2003	13	24.4 ± 11.3	59.2 ± 17.1	4 (30.8)
Bauman et al[32]	2005	11	11.5 ± 5.5	67.3 ± 21.6	5 (45.5)
Iida et al[33]	2005	6	10.7 ± 4.3	25.0 ± 7.3	3 (50.0)
Chuang et al[34]	2006	2	1.5 ± 0.8	6.0 ± 0	0
Costello et al[35]	2005	1	36	16	1 (100)
Behdad et al[36]	2009	6	15.2 ± 1.5	26.0 ± 14.5	3 (50.0)
Nakayama et al[37]	2010	1	7	10	0
Patil et al[38]	2010	10	39.2 ± 9.6	20.7 ± 8.1	6 (66.7)
Wang et al[39]	2013	1	33	17	1 (100)
Patil et al[40]	2013	15	44.4 ± 9.1	39.3 ± 12.2	14 (87.5)
Chen et al[41]	2015	1	11	17	1 (100)
Total		212	20.9 ± 13.7	33.0 ± 20.0	96 (45.3)

[a]Only mean given, so standard deviation not calculable.

(such as Lennox-Gastaut and Landau-Kleffner; 62.5% Engel Class I), and simple partial seizures (57.9%), though these categories had very small sample sizes compared to more common complex and simple partial seizures. Complex partial seizures had some of the worst outcomes in comparison (39.0% Engel class I; Table 3).

The most frequent recorded complications were hemi- and monoparesis, which occurred transiently in 42 patients (26.4%) and remained permanent in 14 patients (6.6%). Language difficulties were the second most common, and were transient in 26 patients (12.3%) and permanent in 4 (1.9%). Other complications are quantified in Table 4.

DISCUSSION

Per guidelines from the American Academy of Neurology, the American Epilepsy Society, and the American Association of Neurological Surgeons, patients with newly diagnosed refractory epilepsy should all be evaluated for potentially curative epilepsy surgery.[42] Though before surgical resection can proceed, the epileptic focus must be adequately localized, typically through imaging, seizure semiology, and electrophysiology.[43,44] Foci localized in noneloquent areas generally can be safely resected, and surgery provides a good chance of seizure freedom for many of these patients.[45-47] The issue becomes complicated, however,

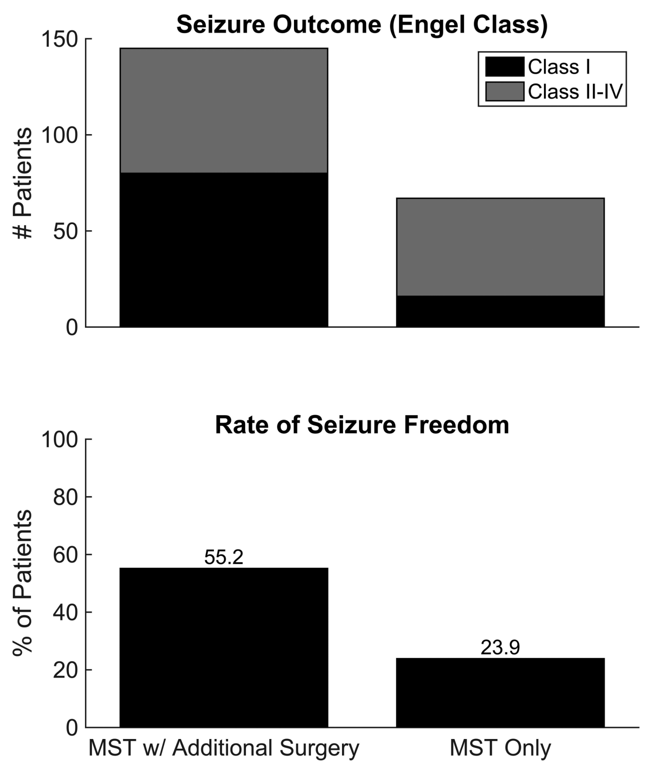

FIGURE 2. *Seizure freedom rates for MST alone and MST combined with surgical resection. The number of patients with different Engel class outcomes for both surgery types (MST + resection and MST alone) are shown in the top panel, with the percentages of each depicted in the bottom panel.*

when seizure foci arise in eloquent areas, making resection untenable given the possibility of causing pronounced permanent neurological deficits.[2]

For these patients with foci in eloquent areas, the technique of MST was introduced by Morrell et al in 1989.[4] As described above, the procedure uses multiple passes of a bent wire probe to interrupt intracortical connections within an epileptic focus, but preserves the subcortical efferent and afferent fibers. This disruption of the focus putatively prevents lateral spread of seizures, but maintains the area's eloquent function. While MST was one of the original treatments for eloquent foci, many novel neuromodulatory treatments now exist, such as VNS, RNS, and DBS, all of which have class I evidence supporting their use.[3] Yet, despite predating each of these neuromodulatory therapies, no comprehensive review of the MST literature exists.

Herein, we conducted a systematic review of literature to create a synthetic cohort of 212 patients undergoing MST. Most of these patients had MST as an adjunct to standard resection, and most of these patients were seizure-free (55.2%). A sizeable portion also had MST alone, without resection, and had a seizure freedom rate of 23.9%. This is notably different than the prior meta-analysis of Spencer et al,[5] wherein 62% of patients with complex partial seizures and 71% of patients with generalized seizures had excellent outcomes following isolated MST (without resection), where "excellent outcome" is defined as a ≥95% reduction in seizures.[5] Even if the Engel class I and II outcomes are combined in our systematic review, the improvement rate we found is significantly lower (41.8% class I or II for isolated MST) than the 62% to 71% reported by Spencer et al.[5] Part of this difference could be related to a volume–outcome relationship, whereby the 6 high-volume centers used in the Spencer et al[5] meta-analysis outperformed the more varied centers represented in the present systematic review, though we cannot analyze this in detail given the lack of volume data for the reviewed studies.[48]

When data were available describing seizure semiology, complex partial seizures had worse outcomes (39.0% Engel class I; Table 3) than simple partial seizures (57.9%), syndromic epilepsy (62.5%), and epilepsia partialis continua (66.7%). Anatomically, however, temporal lobe foci had the best outcomes (OR 4.95, 95% CI 1.71-14.3; Table 2). It should be emphasized that complex partial seizures in general do not arise exclusively from temporal lobe foci (eg, in this cohort 52% of complex partial seizures have nontemporal foci), which helps explain this difference.

Comparison to Other Modalities

Importantly, even if we accept the lower seizure freedom rate of 23.9% reported herein (as opposed to the 62%-71% reported by Spencer et al[5]), this rate is still higher than that of any current neuromodulatory therapy, such as VNS (8.2% seizure freedom at 24 mo[49]), RNS (0% overall at a mean follow-up of 5.4 yr, though 23% of patients have transient 6-mo periods of seizure freedom[50]), or DBS of the anterior nucleus (0% after 5 yr, but 16% with transient 6-mo periods of seizure freedom[51]). Yet, as noted before, the MST patients do worse than standard resection patients, whether for mesial temporal sclerosis (60%-90% seizure freedom) or neocortical epilepsy (40%-70% seizure freedom).[47] However, patients undergoing standard surgical resection generally do not have foci in eloquent locations. There is no patient cohort, to our knowledge, where resection alone was used in eloquent areas, as compared to MST or MST and resection.

While none of the neuromodulation studies above specifically delineate patients with eloquent foci (allowing for a more direct comparison with MST), some inferences can be drawn. For instance, it has been shown that VNS is less likely to be successful with focal epilepsy (eloquent or not), as compared to generalized epilepsy (OR 1.38 favoring generalized, 95% CI 1.06-1.81)[49]. RNS, unlike VNS, requires identification of seizure foci before placement and has not been applied to generalized seizures. Roughly half of the RNS patients treated in the pivotal trial had lateral temporal or extratemporal foci, and many of these foci were likely in eloquent locations (given the choice of RNS over resection), though the publications describing RNS do not specify

TABLE 2. Patient Characteristics and seizure Outcomes for MST

Characteristic	# Class I (%)	# Class II-IV (%)	Total (%)	Odds ratio (95% CI)
Age	23.6 ± 15.8	19.9 ± 11.8	21.6 ± 13.9	$P = .06$
Gender				
Female	36 (37.5)	57 (43.9)	93 (43.9)	1 [reference]
Male	60 (72.5)	59 (50.9)	119 (56.1)	1.61 (0.93, 2.79)
Seizure focus laterality				
Right	38 (39.6)	51 (44.0)	89 (42.2)[a]	1 [reference]
Left	56 (58.3)	60 (51.7)	116 (55.0)[a]	1.25 (0.72, 2.18)
Bilateral	2 (0.1)	4 (0.3)	6 (2.8)[a]	0.67 (0.12, 3.86)
Operation				
MST only	16 (16.7)	51 (44.0)	67 (31.6)	1 [reference]
Without biopsy	14 (14.6)	44 (37.9)	58 (27.4)	
With biopsy	2 (2.1)	7 (6.0)	9 (4.2)	0.90 (0.17, 4.83)
MST + resection	78 (81.3)	64 (55.2)	142 (70.0)	**3.88 (2.02, 7.45)**
MST + disconnection	2 (2.1)	0	2 (0.9)	n/a
MST + VNS	2 (2.1)	0	2 (0.9)	n/a
Focus location				
Frontal	21 (21.9)	24 (20.7)	45 (21.2)	1 [reference]
Temporal	26 (27.1)	6 (5.2)	32 (15.1)	**4.95 (1.71, 14.3)**
Parietal	3 (3.1)	6 (5.2)	9 (4.2)	0.57 (0.13, 2.57)
Occipital	0	1 (0.9)	1 (0.5)	n/a
Frontal-parietal	20 (20.8)	33 (28.4)	53 (25.0)	0.69 (0.31, 1.55)
Frontal-temporal	9 (9.4)	19 (16.4)	28 (13.2)	0.54 (0.20, 1.45)
Temporal-parietal	4 (4.2)	4 (3.4)	8 (3.8)	1.14 (0.25, 5.15)
Temporal-occipital	2 (2.1)	2 (1.7)	4 (1.9)	1.14 (0.15, 8.84)
Parietal-occipital	0	1 (0.9)	1 (0.5)	n/a
Frontal-temporal-parietal	6 (6.3)	14 (12.1)	20 (9.4)	0.49 (0.16, 1.50)
Frontal-temporal-occipital	1 (1.0)	3 (2.6)	4 (1.9)	0.38 (0.04, 3.95)
Temporal-parietal-occipital	2 (2.1)	0	2 (0.9)	n/a
Frontal-parietal-occipital	0	2 (1.7)	2 (0.9)	n/a
All lobes	2 (2.1)	1 (0.9)	3 (1.4)	2.29 (0.19, 27.05)

[a]One patient did not have a laterality reported, so the total number of patients is lower for this category than others. Statistically significant differences are indicated in bold.

TABLE 3. Seizure Types and Outcome. Only Patients With Clear Documented Seizure Types were Included (n = 167; 78.8% of All Patients)

Seizure type	# Patients (%)	# Class I outcome (%)
Simple partial	19 (14.7)	11 (57.9)
Complex partial	77 (59.7)	30 (39.0)
Generalized	10 (7.8)	5 (50.0)
Status	6 (4.7)	3 (50.0)
Epilepsia partialis continua	6 (4.7)	4 (66.7)
Syndromic[a]	8 (6.2)	5 (62.5)
Other[b]	3 (2.3)	1 (33.3)

[a]Includes Lennox-Gastaut and Landau-Kleffner.
[b]Includes drop attacks, atonic seizures, and myoclonic seizures.

TABLE 4. Complications of MST

Complication	# Patients (%)
Paresis	56 (26.4)
Transient	42 (19.8)
Permanent	14 (6.6)
Dysphasia	30 (14.2)
Transient	26 (12.3)
Permanent	4 (1.9)
Visual Field Deficit	14 (6.6)
CSF leak	8 (3.8)
Hematoma	6 (2.8)
Infection	5 (2.4)

CSF, cerebrospinal fluid.

whether foci were eloquent or not. Nevertheless, there was no difference in outcome for patients with temporal vs extratemporal foci, suggesting the overall rate of seizure freedom applies equally to eloquent and noneloquent areas.[50,52] Like RNS, papers describing DBS of the anterior thalamic nucleus do not specify whether the treated seizure foci were eloquent, though ∼20% of patients had "diffuse" or "other" specified as the seizure onset location in the SANTE trial, leaving ∼80% as potential eloquent cases.[53] Again, as for RNS, many of the DBS patients likely had foci in eloquent areas, prompting the choice of DBS over resection, though the exact breakdown is unknown.

Though MST provides a good chance for seizure freedom, neurological complications with MST were more frequent than complications from resective epilepsy surgery. This is likely due to the direct manipulation of eloquent tissue during MST, tissue that is typically spared during traditional resections. For example, transient hemi- and monoparesis afflicted 19.8% of patients, and transient dysphasias 12.3% of patients—these deficits were permanent in 6.6% and 1.9% of patients, respectively (Table 4). In contrast, Hader et al[54] conducted a systematic review of epilepsy surgery complications and found a 3.7% rate of transient dysphasia and 0.8% for permanent dysphasia.[54]

The use of MST should therefore be viewed with the typical risk vs benefit lens of all surgery—while there are greater risks of injury with MST than standard resection, there are potentially greater rewards in terms of seizure freedom if the eloquent area can also be treated, instead of avoided. If a medically refractory seizure focus lies within eloquent cortex, the options are to do nothing, use some form of neuromodulation, attempt MST, or resect the eloquent area and accept a neurological deficit. Each option adds progressively more risk, but offers progressively higher odds of seizure freedom. If the goal is weighted toward seizure freedom, the studies reviewed herein would suggest the focus be resected to the limits of eloquent cortex, followed by MST in the remaining eloquent areas. However, if the potential for neurological deficits is too worrisome, then a form of nonresective neuromodulation will be more appropriate.

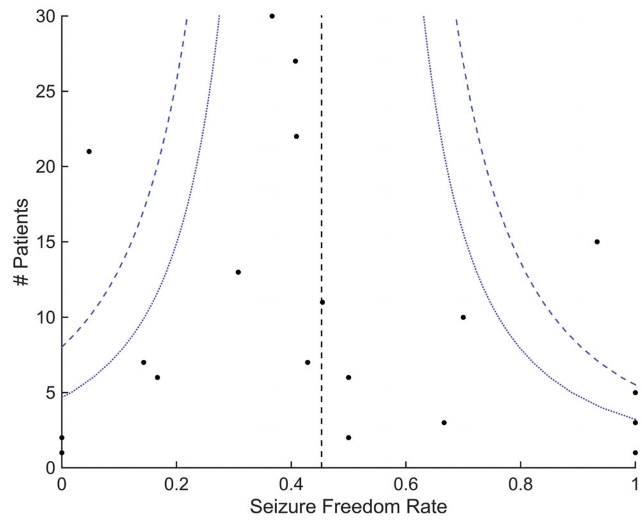

FIGURE 3. *Funnel plot of study data. Studies are plotted based on study size (# patients) and reported seizure freedom rate. The average across the synthetic cohort (45.3%) is plotted as a vertical dashed line. The 95% confidence intervals are shown as dotted lines and 99% confidence intervals as dashed lines.*

Limitations

There are several limitations to these conclusions. First, there is no class I evidence for the use of MST. This is not the case for open surgical resection,[45,46] VNS,[55] DBS,[53] or RNS,[52] which all have randomized-controlled trials supporting their efficacy.[3] While many studies argue for the utility of MST, the lack of randomized trials suggests that the efficacy of MST might be inflated by the selection and reporting biases inherent to small case series. However, a funnel plot of the data (Figure 3) shows a symmetric distribution with all but 3 studies within the 95% confidence limits of the expected average, suggesting no obvious reporting bias. As another means of testing for reporting bias, we excluded the 16 smallest case series, which negligibly changed the seizure freedom rate from 45.3% to 42.3%, largely because these small studies only account for a small portion of the reported cases (16 of 212, or 7.5%).

Second, the reporting of complications in the reviewed studies was not standardized or verified, and, in particular, many studies did not document neuropsychological testing. The actual presence of neurological deficits postoperatively might therefore be higher than presented here, particularly for subtler and harder to detect cognitive issues. Prospective trials with strict criteria for monitoring complications and for evaluating neuropsychological outcomes is the best means for addressing this.

Third, while the above data compare resection plus MST to MST alone, there is no comparable group of patients undergoing resection alone in eloquent areas (without any MST). Without that comparison, it is difficult to know what value MST adds to resection, and therefore whether it is worth the additional risks. On the other hand, because the above data show that MST in isolation is quite powerful—23.9% seizure freedom—MST likely does function as a useful adjunct, though again without direct comparisons there is no way to know the magnitude of this effect.

Lastly, all literature reviews have inherent limitations when combining heterogeneous patient populations, surgical techniques, reporting standards, and follow-up times, which can bias the resulting outcomes.[56] Again, the best alternative is to conduct controlled studies in the future, and to require strict reporting standards for future case series.

CONCLUSION

Patients with seizure foci in eloquent areas are often not candidates for traditional surgical resection. MST is one method for treating these patients, with a seizure freedom rate of 55.2% when MST is combined with resection and 23.9% when used alone. Importantly, these seizure freedom rates are far higher than those of neuromodulatory therapies such as VNS, DBS, or RNS, though the surgery clearly carries higher risk: neurological complications from MST appear to be more frequent than with traditional resection or neuromodulatory therapies, with transient mono- or hemiparesis occurring in 19.8% of patients, transient dysphasias in 12.3%, and permanent paresis and dysphasis in 6.6% and 1.9% of patients, respectively. The greatest limitation of MST is the lack of class I evidence validating its efficacy and complication rates, which would help establish its place in the treatment of eloquent seizure foci.

Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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COMMENT

The authors present a well written systematic review on multiple subpial transections for medically intractable epilepsy using the PRISMA reporting guideline. The systematic review fulfills the PRISMA guideline well, though the available data in the literature is sparse. The review covers an important topic that has not received the research attention it deserves as of late. It is a reminder that while neuromodulation has its merits, there remains another option.

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