Neurosurgical Forum LETTERS TO THE EDITOR

Deep brain stimulation for schizophrenia

TO THE EDITOR: We read with great interest the review by Mikell et al.³ (Mikell CB, Sinha S, Sheth SA: Neurosurgery for schizophrenia: an update on pathophysiology and a novel therapeutic target. *J Neurosurg* 124:917–928, April 2016). These authors summarize current understanding of the pathophysiology of schizophrenia based on dysfunction in dopaminergic and glutamatergic signaling. They suggest several nodes of the basal ganglia–thalamocortical circuit as therapeutic targets for deep brain stimulation (DBS): the hippocampus, the ventral striatum, and the associative striatum.³ Regarding this dopamine dysregulation–based hypothesis, we believe that there are other targets that could be useful for DBS: the mediodorsal thalamus and the internal globus pallidus.^{1,4,5,9} Moreover, in the last few years, findings from voxel-based morphometry, diffusion tensor imaging, and functional MRI suggest structure and functional alterations of the medial prefrontal cortex, specifically the area correlated to the anterior midline node of the default mode network.^{6,8} This area corresponds to the subcallosal cingulate gyrus, which includes Brodmann area 25. The failure of task-related deactivation in this medial frontal cortex is related to the symptoms of schizophrenia. Actually, a meta-analysis of the whole-brain voxel-based approach revealed that abnormalities in white matter areas in schizophrenia were consistently identified across the studies in only 2 locations, one of them corresponding to this anterior cingulate subgenual area.² This region has been stimulated with DBS in other neuropsychiatric disorders, and in our experience in treatment-resistant depression, no associated complications have been observed.⁷ We suggest that this could be another possible target for the treatment of resistant schizophrenia.

Schizophrenia remains one of the leading causes of disability worldwide, with 30% of patients refractory to treatment. We agree that given the severity of this disease and its high consumption of resources, new treatment strategies are needed. We are conducting a prospective, randomized, double-blind clinical trial (clinical trial no.: NCT02377505, clinicaltrials.gov) aimed at assessing the tolerability and efficacy of DBS in refractory schizophrenia (funding Grant Nos. PI12/00042 [E.A.] and PI12/00686 [S.S.] from the Instituto de Salud Carlos III).

We randomized the therapeutic target (nucleus accumbens vs subgenual area), and after the start of stimulation and a period of clinical stability, we made a crossover phase of generator on or off. We are studying treatment response in terms of neuroimaging (MRI, PET) and clinical variables. Completion of this ongoing study and an exhaustive analysis of the data are needed for definitive answers.

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References

1. Buchmann A, Denticio D, Peterson MJ, Riedner BA, Sarasso S, Massimini M, et al: Reduced mediodorsal thalamic volume and prefrontal cortical spindle activity in schizophrenia. *Neuroimage* 102:540–547, 2014
2. Ellison-Wright I, Bullmore E: Meta-analysis of diffusion tensor imaging studies in schizophrenia. *Schizophr Res* 108:3–10, 2009
3. Mikell CB, Sinha S, Sheth SA: Neurosurgery for schizophrenia: an update on pathophysiology and a novel therapeutic target. *J Neurosurg* 124:917–928, 2016
4. Mwansisya TE, Wang Z, Tao H, Zhang H, Hu A, Guo S, et al: The diminished interhemispheric connectivity correlates with negative symptoms and cognitive impairment in first-episode schizophrenia. *Schizophr Res* 150:144–150, 2013
5. Oertel-Knöchel V, Knöchel C, Matura S, Rotarska-Jagiela A, Magerkurth J, Prvulovic D: Cortical-basal ganglia imbalance in schizophrenia patients and unaffected first-degree relatives. *Schizophr Res* 138:120–127, 2012
6. Pomarol-Clotet E, Salvador R, Sarró S, Gomar J, Vila F, Martínez A, et al: Failure to deactivate in the prefrontal cortex in schizophrenia: dysfunction of the default mode network? *Psychol Med* 38:1185–1193, 2008

7. Puigdemont D, Portella M, Pérez-Egea R, Molet J, Gironell A, de Diego-Adeliño J, et al: A randomized double-blind crossover trial of deep brain stimulation of the subcallosal cingulate gyrus in patients with treatment-resistant depression: a pilot study of relapse prevention. **J Psychiatry Neurosci** 40:224–231, 2015
8. Salgado-Pineda P, Fakra E, Delaveau P, McKenna PJ, Pomarol-Clotet E, Blin O: Correlated structural and functional brain abnormalities in the default mode network in schizophrenia patients. **Schizophr Res** 125:101–109, 2011
9. Young KA, Manaye KF, Liang C, Hicks PB, German DC: Reduced number of mediodorsal and anterior thalamic neurons in schizophrenia. **Biol Psychiatry** 47:944–953, 2000

Disclosures

The authors report no conflict of interest.

Response

We thank the authors for their interest in our article. We are intrigued by the suggestion of the subgenual anterior cingulate cortex (Cg25) as a potential therapeutic target. Evidence from the original trial of DBS for depression¹ indicating that Cg25 stimulation boosted dorsolateral prefrontal cortex and dorsal anterior cingulate cortex blood flow seems consistent with the idea that stimulation of this area could treat the frontal dysfunction observed in schizophrenia. We eagerly await the results of the authors' trial and agree that further work is needed to understand this difficult disease.

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References

1. Mayberg HS, Lozano AM, Voon V, McNeely HE, Seminowicz D, Hamani C, et al: Deep brain stimulation for treatment-resistant depression. **Neuron** 45:651–660, 2005

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Failed microvascular decompression surgery

TO THE EDITOR: I read the article by Bigder and Kaufmann² with great interest (Bigder MG, Kaufmann AM: Failed microvascular decompression surgery for hemifacial spasm due to persistent neurovascular compression: an analysis of reoperations. *J Neurosurg* 124:90–95, January 2016). I would like to address several comments to the authors. In the article, the authors mentioned that microvascular decompression (MVD) is no guarantee of a hemifacial spasm (HFS) cure, presumably given a failure rate of nearly 10%. Despite all our efforts, we do know that there is a discrepancy between technical and clinical success in the operation; that is, the surgeons are quite

sure of decompression during the surgery, but the clinical results do not always correspond. In this respect I agree with the authors. However, I do wonder what rate of failure would fulfill the authors' guarantee of success because I believe that our mission continues to be improvement of the surgery as long as MVD is the only curative treatment for HFS.

Previously, in a report on patients with trigeminal neuralgia in whom treatment had failed, Jannetta and Bissonette described, "a 'failed' patient is a signal that we are not perfect and that the forces of nature have again outwitted us. We cannot hide these failures, avoid them, or ignore them. Rather, we can learn from them and, frequently, can make the patients feel better or even cure them."³⁴ The article by Bigder and Kaufmann illustrates 3 important points that can help us achieve better outcomes. Firstly, exposure of the sigmoid sinus and inferior floor of the cerebellum should never be skipped. Secondly, the vertebral artery should be properly transposed but not interposed. Thirdly, we should try our best to mobilize the responsible artery in the presence of perforating arteries. I fully agree with their conclusion that caudal side exposure is very important for observation of the entire facial nerve as well as the protection of hearing function.¹ In addition, I mobilize the arterial loops close to the facial root exit zone (fREZ) that represent potential causes of HFS in the future to avoid new neurovascular compression, if this maneuver can be achieved safely. I believe that correct application of all these procedures in the initial surgery will increase the rate of success.

Finally, I would like to discuss the importance of preoperative imaging, which the authors did not mention in their article. The techniques of preoperative MRI are well advanced and established.³ However, I am afraid that neurosurgeons may depend on MRI too much. Vascular components can be located nearby or even conflict with the seventh and eighth cranial nerve complex in the absence of symptoms and can represent the cisternal part that is not responsible for the symptoms in patients with HFS. Consequently, the proximal part of the fREZ may be overlooked.

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References

1. Amagasaki K, Watanabe S, Naemura K, Nakaguchi H: Microvascular decompression for hemifacial spasm: how can we protect auditory function? **Br J Neurosurg** 29:347–352, 2015
2. Bigder MG, Kaufmann AM: Failed microvascular decompression surgery for hemifacial spasm due to persistent neurovascular compression: an analysis of reoperations. **J Neurosurg** 124:90–95, 2016
3. Du ZY, Gao X, Zhang XL, Wang ZQ, Tang WJ: Preoperative evaluation of neurovascular relationships for microvascular decompression in the cerebellopontine angle in a virtual reality environment. **J Neurosurg** 113:479–485, 2010
4. Jannetta PJ, Bissonette DJ: Management of the failed patient with trigeminal neuralgia. **Clin Neurosurg** 32:334–347, 1985

Disclosures

The author reports no conflict of interest.

Response

We thank Dr. Amagasaki for his thoughtful comments regarding MVD for HFS. The objective of our paper was to highlight what we perceived to be a frequent source of failed surgery: incomplete exposure, exploration, and decompression of the fREZ. The successful alleviation of the compression caused by culprit vessels is associated with a high rate of disease cure. We also agree that vessels “that represent potential causes of HFS in the future” should be similarly mobilized or transposed when it can be safely achieved during surgery.

Regarding preoperative diagnostic imaging, it is not uncommon for dictated reports to describe the common association between vessels and the cisternal portion of the facial nerve, which is usually incidental, whereas the culprit neurovascular compression at the fREZ is not noted. We have previously reported on the nature of this compression causing HFS and agree that high-resolution imaging has a very high degree of sensitivity when carefully interpreted.¹ Such imaging has also been quite useful in the evaluation of patients with persisting spasms after MVD surgery. In our paper we referenced 2 such cases (Cases 3 and 5) in which previously unidentified neurovascular compression was clearly evident following the first surgery and supported early reoperation.

It also bears emphasizing that HFS cure sometimes follows a latency period of several months, even more than 1 year, after technically effective alleviation in culprit neurovascular compression.^{2–5} Reoperations in such cases are unnecessary and subject the patient to unnecessary surgical risks. It is our practice to offer reoperation for persisting spasms within the 1st year only if persisting vascular compression on the fREZ is demonstrable on high-resolution MRI. The majority of patients will, however, demonstrate immediate or gradual resolution of HFSs in the first few months following technically thorough MVD surgery.

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References

1. Campos-Benitez M, Kaufmann AM: Neurovascular compression findings in hemifacial spasm. *J Neurosurg* **109**:416–420, 2008
2. Dai Y, Ni H, Xu W, Lu T, Liang W: Clinical analysis of hemifacial spasm patients with delay symptom relief after microvascular decompression of distinct offending vessels. *Acta Neurol Belg* **116**:53–56, 2016
3. Li CS: Varied patterns of postoperative course of disappearance of hemifacial spasm after microvascular decompression. *Acta Neurochir (Wien)* **147**:617–620, 2005
4. Oh ET, Kim E, Hyun DK, Yoon SH, Park H, Park HC: Time course of symptom disappearance after microvascular decompression for hemifacial spasm. *J Korean Neurosurg Soc* **44**:245–248, 2008
5. Shin JC, Chung UH, Kim YC, Park CI: Prospective study

of microvascular decompression in hemifacial spasm. *Neurosurgery* **40**:730–735, 1997

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Dural arteriovenous fistula mimicking Creutzfeldt-Jakob disease

TO THE EDITOR: We read with great interest the report by Holekamp et al.¹ on dural arteriovenous fistula (dAVF)–induced thalamic dementia (Holekamp TF, Mollman ME, Murphy RKJ, et al: Dural arteriovenous fistula–induced thalamic dementia: report of 4 cases. *J Neurosurg* **124**:1752–1765, June 2016). We similarly had a 61-year-old male patient with no significant medical history who was being screened for subacute-onset dementia. On MRI, he had bithalamic T2 hyperintensity without restricted diffusion (Fig. 1). Physicians at another institution suspected that the patient had Creutzfeldt-Jakob disease when he suddenly developed coma and intraventricular hemorrhage on CT scans (Fig. 2). This resulted in emergency neurosurgical transfer to our institution for a vascular evaluation and emergency diagnostic cerebral digital subtraction angiog-

FIG. 1. A: Axial MR image obtained without contrast. B: T2-weighted spin echo MR image demonstrating bithalamic hyperintensities. C: Axial MR image showing no diffusion-weighted restriction. D: MR angiogram showing tortuous, curvilinear vessel extending posteriorly and inferiorly from the area of the vein of Galen (arrow).

FIG. 2. Axial CT scan of the head obtained without contrast showing acute development of left medial thalamic hemorrhage with intraventricular hemorrhage.

raphy (DSA) (Fig. 3). We discovered a Borden II/Cognard IIb stage dAVF in this patient. The dAVF was treated with immediate angiographic embolization and obliteration. The patient regained consciousness but had cognitive impairment. He was later discharged to inpatient rehabilitation. We think that similar dAVF cases that cause venous hypertension or vascular steal on the bilateral thalami have a characteristic MRI presentation. In such cases, MR angiography could be useful to screen for a dAVF.

FIG. 3. **Left:** DSA study of the right external carotid artery demonstrating a dAVF (arrowhead) with draining vein and feeding arteries from the posterior meningeal artery (white arrow) and feeding arteries from the occipital artery (black arrows). **Right:** DSA study obtained after Onyx embolization of the aforementioned feeding arteries, showing complete obliteration of the dAVF.

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References

1. Holekamp TF, Mollman ME, Murphy RKJ, Kolar GR, Kramer NM, Derdeyn CP, et al: Dural arteriovenous fistula–induced thalamic dementia: report of 4 cases. *J Neurosurg* [epub ahead of print November 20, 2015. DOI: 10.3171/2015.5.JNS15473]

Disclosures

Dr. Tawk has direct stock ownership in Blockade Medical.

Response

My coauthors and I greatly appreciate the insightful comments from Dr. Freeman and his colleagues. Their case nicely demonstrates two important characteristics of patients with dAVF-induced thalamic dementia highlighted in our article: 1) the typical MRI finding of bithalamic hyperintensities on T2/FLAIR studies without associated restricted diffusion; and 2) the common occurrence of a significant delay between symptom onset and diagnosis in these patients. In their particular case, the diagnosis was not made until a precipitous decline in the patient's neurological condition due to intraventricular hemorrhage prompted transfer to the authors' hospital. This aggressive clinical course is an important reminder of the well-documented poor natural history associated with dAVFs presenting with symptomatic cortical venous drainage^{1–3}—a natural history that argues strongly for prompt treatment of these lesions following initial diagnosis.⁴ Finally, the authors correctly point out that noninvasive vascular imaging studies such as MR angiography or CT angiography can play an important role in the identification of dAVFs—especially those having cortical venous drainage.

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References

1. Gross BA, Du R: The natural history of cerebral dural arteriovenous fistulae. *Neurosurgery* **71**:594–603, 2012
2. Söderman M, Pavic L, Edner G, Holmin S, Andersson T: Natural history of dural arteriovenous shunts. *Stroke* **39**:1735–1739, 2008
3. Strom RG, Botros JA, Refai D, Moran CJ, Cross DT III, Chicoine MR, et al: Cranial dural arteriovenous fistulae: asymptomatic cortical venous drainage portends less aggressive clinical course. *Neurosurgery* **64**:241–248, 2009
4. Zipfel GJ, Shah MN, Refai D, Dacey RG Jr, Derdeyn CP: Cranial dural arteriovenous fistulas: modification of angiographic classification scales based on new natural history data. *Neurosurg Focus* **26**(5):E14, 2009

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The role of neurosurgeons in mild traumatic brain injury

TO THE EDITOR: We read with interest the article by Ditty et al.² (Ditty BJ, Omar NB, Foreman PM, et al: The nonsurgical nature of patients with subarachnoid or intraparenchymal hemorrhage associated with mild traumatic brain injury. *J Neurosurg* 123:649–653, September 2015). The authors presented a retrospective review of 500 consecutively treated patients with mild traumatic brain injury (mTBI) and imaging findings of traumatic subarachnoid hemorrhage (tSAH) and/or intraparenchymal hemorrhage (IPH) and concluded that such patients require neither neurosurgical consultation nor transfer to tertiary care referral centers. The solution they proposed, which excludes the need for neurosurgeons in the management of mTBI, may be reasonable in rural areas where transfer to a neurosurgically equipped center may be difficult or delay patient care. However, we believe that the exclusion of neurosurgical consultation should be the exception rather than the rule. At Level I and Level II trauma centers, especially those with major academic centers, neurosurgery should continue to be involved in the care of patients with mTBI and can do so without excess cost. Ceding the care of these patients to other services may result in worse patient care, worse neurosurgical resident training, and fewer research opportunities to advance the field of TBI.

The authors' report primarily focused on cost and the allocation of resources. A related article by Joseph et al. emphasized the consult burden faced by neurosurgeons and reached the same conclusion.³ Overall, cost is certainly a consideration; however, excluding neurosurgeons from the management of mTBI is not necessary for cost containment. Alternatively, Carlson et al. proposed a preferable model utilizing initial telephone triage by a neurosurgeon without interhospital transfer.¹ Traumatic SAH can be managed by neurosurgeons at a low cost by the judicious use of imaging and intensive care unit admission.⁴

Traumatic brain injury is necessarily a neurosurgical pathology. Most neurosurgical diseases span a broad spectrum of care that includes both operative and nonoperative management. For example, in the treatment of brain tumors or vascular malformations, the neurosurgeon is responsible for the clinical and radiographic findings that merit surgical versus conservative management because only the neurosurgeon can perform surgery should it become necessary. The neurosurgeon is also best suited and most experienced for the long-term follow-up of such patients. There can be significant sequelae in "mild" TBI and tSAH and/or IPH, both in the short- and long-term; therefore, neurosurgeons who have been trained in managing mTBI patients and who understand the complex neuropsychological sequelae must be involved in the care of these patients.⁵

Moreover, excluding neurosurgeons in the management of mTBI at centers with neurosurgical residency programs significantly erodes the quality of training. Trainees cannot learn to judiciously choose operative management if they are not exposed to nonoperative management. Neurosurgical trainees must see the full spectrum of TBI and understand the nuanced decision-making process in neu-

rotrauma. Otherwise, we devolve from physicians to protocol-driven technicians.

The effect that deferring neurosurgical consultation of mTBI patients has on neurotrauma research must also be considered. Neurosurgeons have long been involved in advancing the field of TBI and treatment, and even currently, they have a demonstrated interest in pathologies such as concussions that have a "nonsurgical nature." Without evidence of hemorrhage on imaging, concussions are arguably milder than the mTBI and tSAH discussed by Ditty et al. To continue their involvement in research and in treating concussions, neurosurgeons must maintain their visibility among physician peers by being present in the patient care of all TBI, from mild to severe.

Since the American College of Emergency Physicians and Centers for Disease Control and Prevention have not set forth specific guidelines for the management of mild intracranial bleeds, organized neurosurgery should lead the development of such guidelines, so that patients with TBI are not improperly managed.

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References

1. Carlson AP, Ramirez P, Kennedy G, McLean AR, Murray-Kreznar C, Stippler M: Low rate of delayed deterioration requiring surgical treatment in patients transferred to a tertiary care center for mild traumatic brain injury. *Neurosurg Focus* 29(5):E3, 2010
2. Ditty BJ, Omar NB, Foreman PM, Patel DM, Pritchard PR, Okor MO: The nonsurgical nature of patients with subarachnoid or intraparenchymal hemorrhage associated with mild traumatic brain injury. *J Neurosurg* 123:649–653, 2015
3. Joseph B, Pandit V, Haider AA, Kulvatunyou N, Zangbar B, Tang A, et al: Improving hospital quality and costs in nonoperative traumatic brain injury: the role of acute care surgeons. *JAMA Surg* 150:866–872, 2015
4. Quigley MR, Chew BG, Swartz CE, Wilberger JE: The clinical significance of isolated traumatic subarachnoid hemorrhage. *J Trauma Acute Care Surg* 74:581–584, 2013
5. Rabinowitz AR, Li X, McCauley SR, Wilde EA, Barnes A, Hanten G, et al: Prevalence and predictors of poor recovery from mild traumatic brain injury. *J Neurotrauma* 32:1488–1496, 2015

Disclosures

The authors report no conflict of interest.

Response

No response was received from the authors of the original article.

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Topical vancomycin use following craniotomy

TO THE EDITOR: We read with keen interest the article by Abdullah et al.¹ regarding the use of topical vancomycin in reducing surgical site infections (SSIs) following craniotomy (Abdullah KG, Attiah MA, Olsen AS, et al: Reducing surgical site infections following craniotomy: examination of the use of topical vancomycin. *J Neurosurg* 123:1600–1604, December 2015). We commend the authors for describing a method to decrease SSIs following craniotomy, which remain an important preventable cause of morbidity and mortality in neurosurgical practice. The authors describe 150 consecutive patients who underwent craniotomy, in which the first 75 patients did not receive topical vancomycin (control group) and the subsequent 75 patients received 1 g of topical vancomycin. The incidence of SSIs was significantly less in the vancomycin group. Topical vancomycin is well established to decrease SSIs in spinal surgeries.^{3,7} Although topical vancomycin is used in intracranial surgeries by many surgeons, this is the first study showing its efficacy following craniotomy.

The readers would be interested to know what was included in SSIs in the study, because SSIs have not been defined in the study. The exclusion criteria are not mentioned.

There are many confounding factors that might affect the rates of infection and that should be considered while studying infection rates in intracranial surgeries. These factors include preoperative CSF diversion via external ventricular drain and postoperative CSF leaks.^{2,4,5} The use of Gliadel wafers in gliomas is known to have a higher incidence of SSIs.⁶ Patients with an allergy to penicillin received injectable vancomycin as preoperative prophylaxis and also in the postoperative period. The number of such patients in each group has not been mentioned and it could be a cause of bias in this study.

Although all patients in the vancomycin group received 1 g of topical vancomycin, the local concentration of the agent is expected to be different in different patients because the surface area of the bone exposed in each surgery is different. One patient in the vancomycin group developed an SSI, and it would be worthwhile to know the surface area of the exposed bone in this patient, because a low concentration of vancomycin might be responsible for the infection. Similarly, it would be important to know the vancomycin drain level in this patient; it may again point out the reason for infection despite application of topical vancomycin.

It is important to know whether or not the organisms cultured from the patients were sensitive to vancomycin, to validate the utility of vancomycin in preventing SSIs in cranial surgeries. It is also important to know whether or not the methicillin-susceptible *Staphylococcus aureus* found in the patient with an SSI in the topical vancomycin group was sensitive to vancomycin.

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References

1. Abdullah KG, Attiah MA, Olsen AS, Richardson A, Lucas TH: Reducing surgical site infections following craniotomy: examination of the use of topical vancomycin. *J Neurosurg* 123:1600–1604, 2015
2. Chiang HY, Kamath AS, Pottinger JM, Greenlee JDW, Howard MA III, Cavanaugh JE, et al: Risk factors and outcomes associated with surgical site infections after craniotomy or craniectomy. *J Neurosurg* 120:509–521, 2014
3. Hill BW, Emohare O, Song B, Davis R, Kang MM: The use of vancomycin powder reduces surgical reoperation in posterior instrumented and noninstrumented spinal surgery. *Acta Neurochir (Wien)* 156:749–754, 2014
4. Korinek AM: Risk factors for neurosurgical site infections after craniotomy: a prospective multicenter study of 2944 patients. The French Study Group of Neurosurgical Infections, the SEHP, and the C-CLIN Paris-Nord. Service Epidémiologie Hygiène et Prévention. *Neurosurgery* 41:1073–1081, 1997
5. Korinek AM, Golmard JL, Elcheick A, Bismuth R, van Effenterre R, Coriat P, et al: Risk factors for neurosurgical site infections after craniotomy: a critical reappraisal of antibiotic prophylaxis on 4,578 patients. *Br J Neurosurg* 19:155–162, 2005
6. McGovern PC, Lautenbach E, Brennan PJ, Lustig RA, Fishman NO: Risk factors for postcraniotomy surgical site infection after 1,3-bis (2-chloroethyl)-1-nitrosourea (Gliadel) wafer placement. *Clin Infect Dis* 36:759–765, 2003
7. Sweet FA, Roh M, Sliva C: Intrawound application of vancomycin for prophylaxis in instrumented thoracolumbar fusions: efficacy, drug levels, and patient outcomes. *Spine (Phila Pa 1976)* 36:2084–2088, 2011

Disclosures

The authors report no conflict of interest.

Response

We very much appreciate the interest in our study and the opportunity to address these thoughtful remarks. First, we considered an SSI to have occurred in any patient readmitted as an inpatient for a surgical wound revision. Our exclusion criteria were patients under the age of 18 years, those who had a “clean contaminated” or “dirty” designation for their index surgery, or any patient undergoing bur hole craniotomy only (including shunts).

Regarding the factors that may confound rates of infection, we agree that these may be multifactorial and sometimes difficult to capture. It so happened that in this study no patients had preoperative CSF diversion, clinically apparent leaking postoperatively, or Gliadel wafer use. An analysis of the use of preoperative intravenous antibiotics and its correlation to infection with or without vancomycin powder as an adjunct is an interesting consideration, and one that we will examine in future studies. We feel similarly regarding the classification of craniotomy size and its correlation to infection. The lone patient who experienced an SSI following craniotomy and vancomycin administration had a standard parietoccipital craniotomy, but the size of the bone flap was not measured in any case in this series. However, we believe that the concentration of 1 g of vancomycin should more than likely suffice for even larger craniotomies, including decompressive procedures (which were present in this series), because the evidence

from spine surgeries has shown that 1 g of vancomycin can still result in high local concentrations in an ostensibly much larger wound.¹

To address the final point, all cultures taken from infected cases grew vancomycin-sensitive organisms. Nonetheless, we agree with the comments from our colleagues—findings regarding the utility of topical vancomycin have been interesting thus far, but require further study. We thank them again for the opportunity to address their well-measured inquiries.

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References

1. Armaghani SJ, Menge TJ, Lovejoy SA, Mencia GA, Martus JE: Safety of topical vancomycin for pediatric spinal deformity: non-toxic serum levels with supratherapeutic drain levels. *Spine (Phila Pa 1976)* 15:1683–1687, 2014

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Augmented reality–guided neurosurgery

TO THE EDITOR: We read with interest the paper by Besharati Tabrizi and Mahvash² that was recently published in this prestigious journal, in which the authors described the in vitro testing and clinical application of a projector-based augmented reality (AR) system (Besharati Tabrizi L, Mahvash M: Augmented reality–guided neurosurgery: accuracy and intraoperative application of an image projection technique. *J Neurosurg* 123:206–211, July 2015). We recently published a paper demonstrating that the registration of rigid bodies as done in Besharati Tabrizi and Mahvash's article, when manually performed under a specific AR visualization, can be guaranteed by optical and geometrical rules,³ and we applied this approach to a maxillofacial procedure.¹

To enhance the value of Besharati Tabrizi and Mahvash's work,² we would like to open a constructive discussion with the authors, and with other experts on this matter, on 2 topics related to the perception of the AR visualization and to the method adopted to evaluate the projection error by the authors.

The first topic is related to the virtual content and the user's perception of it. The system presented by the authors projects a virtual rendering of brain tumors on the patient's head "to plan the skin incision and the craniotomy and to visualize the tumor borders on the brain surface after dural opening." In the *Discussion* section the authors state, "The image projection technique can be used for a 'tailored' skin incision and craniotomy" and then, "Fur-

thermore subcortical lesions, which are not visible on the brain surface during surgery, can be visualized due to lesion projection on the brain surface while planning the approach and operative strategy." They also point out some limits of their approach, such as depth perception of the virtual regions of interest (ROIs): "Depth visualization of ROIs is still a challenge in projecting 2D images." Furthermore, they state that the projector "requires a direct line of sight, which may interfere with the surgeon, the microscope, and the instruments."

Nevertheless, the authors did not explicitly mention a fundamental limit of their system, which is related to the parallax error. As stated in the paper by Gavaghan et al.⁴ cited by the authors, which describes the implementation of the same projector-based AR approach, "all applications displaying structures that are positioned below the projection surface will however be affected by the pose of the viewer." This means that after a proper registration, the location of a projected internal ROI (e.g., a brain tumor) is perceptually consistent only if observed from a viewpoint coincident to that of the projector. This condition is clearly impossible to obtain given the presence of the projector. If the observer's viewpoint does not coincide with that of the projector, the surgeon's perception of the ROI is affected by a parallax error that increases with increasing ROI depth (or increasing surgeon/projector misalignment).

The parallax problem can be easily demonstrated by applying simple geometrical rules that we prefer to skip in this letter, given the clinical scope of this journal. Given the existence of such parallax error, if the surgeon uses the projection of an internal ROI "to plan the skin incision and the craniotomy" he/she will make an error because the ROI (e.g., a tumor) does not lie on the line of sight passing through the observer's eye and the projection of the tumor on the patient's head. It is particularly important to inform the surgeon about the existence of such error, especially for targeting of deep lesions where the parallax error is bigger. For applications in which all visualization data are defined on the head's surface, the procedure's accuracy is not affected by such parallax error.⁴ For this reason, the functionalities presented as future works by the authors will work without any parallax error: "we believe that the described technique can be used very well to quickly and accurately guide surgery for deep brain tumors—not to project the deep tumor borders but to project the preoperatively planned approach and the craniotomy borders or any other useful information to the patient's head, skull, or brain surface."

The second topic is related to the evaluation of the projection error performed by the authors both on the phantom and during real neurosurgical interventions.

On the phantom, "A virtual image was created using a digital photograph of the head phantom with the fiducial markers. The photograph was taken from the same perspective used for image projection. Brain tumors were drawn in the different areas using image editing software." In other words, on the phantom the virtual information does not consist of a virtual 3D model, but is drawn by the user on a 2D picture of the phantom. Projection error is defined as "the difference between the distance of the 5 fiducial markers from the tumor borders on the virtual image and the distance of the 5 fiducial markers from the

tumor borders on the head phantom,” and it is calculated after each manual registration. The authors performed projection accuracy evaluation in 10 cases. In our view, this evaluation is incorrect. We cannot compare measurements done on the virtual image, that represent a 2D projection of the world, with measurements done on the head surface, as shown in Fig. 1C. This problem is probably known by the authors, who state: “Given the anticipated incongruence between the projected 2D virtual image and the 3D convexity of the head, the error of projection after each registration was measured.” It is of fundamental importance to highlight that such measure of projection error is inconsistent because it is influenced by the curvature of the head around the tumor. For this reason the projection error of the different surgical cases cannot be compared because it is affected by the tumor and by the markers’ arrangement for each specific case.

During real neurosurgical interventions, the projection error is evaluated by means of a commercially available neuronavigator. It is our understanding that prior to the intervention, an MRI-based virtual 3D model of the anatomy is registered to the patient independently by the projector-based AR system and by using a common registration routine of the neuronavigator. In Fig. 3C a “navigation pointer” is placed on the border of the tumor projected on the patient’s head surface, as described in the caption: “Accuracy was evaluated using a standard navigation system (navigation pointer) comparing the tumor borders and localization with the MRI on the navigation monitor.” Furthermore, the authors add that “the navigated pointer was used to delineate the tumor borders (anterior, posterior, superior, and inferior) identified with navigation MR images on the navigation monitor...” and “The difference between the tumor borders visualized with image projection and the navigated localization of the tumor borders (navigation pointer) was measured.”

Therefore, it is our understanding that the authors compared the position of 4 points on the head surface corresponding to the projected tumor borders (probably identified by the surgeon as anterior, posterior, superior, and inferior) with their corresponding positions measured on the MR image. The measurement of the distance between reference points on the anatomy and their corresponding points on the MR image is a common approach used to evaluate the target registration error of any surgical navigation modality. In any case, one cannot determine on the MR image shown on the “navigation monitor” the 4 points on the head surface corresponding to the projection of the tumor borders but at most the 3D points (voxel) belonging to the tumor itself. To understand the relevance of results reported during real interventions, it would be fundamental to know exactly how the authors determined the projection error.

We hope to have initiated a productive discussion on this interesting projector-based AR approach to neuro-navigation.

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References

1. Badiali G, Ferrari V, Cutolo F, Freschi C, Caramella D, Bianchi A, et al: Augmented reality as an aid in maxillofacial surgery: Validation of a wearable system allowing maxillary repositioning. *J Craniomaxillofac Surg* 42:1970–1976, 2014
2. Besharati Tabrizi L, Mahvash M: Augmented reality-guided neurosurgery: accuracy and intraoperative application of an image projection technique. *J Neurosurg* 123:206–211, 2015
3. Cutolo F, Badiali G, Ferrari V: Human-PnP: Ergonomic AR interaction paradigm for manual placement of rigid bodies, in Linte CA, Yaniv Z, Fallavollita P (eds): *Augmented Environments for Computer-Assisted Interventions*. Vienna: Springer, 2015, pp 50–60
4. Gavaghan K, Oliveira-Santos T, Peterhans M, Reyes M, Kim H, Anderegg S, et al: Evaluation of a portable image overlay projector for the visualisation of surgical navigation data: phantom studies. *Int J Comput Assist Radiol Surg* 7:547–556, 2012

Disclosures

The authors report no conflict of interest.

Response

We read with interest Ferrari and Cutolo’s letter to the editor, and here is our response. The authors of the letter discussed 2 main issues: 1) parallax effect, and 2) measurement of the projection error.

1. In our paper we discussed the limitation of the projection to depth structures: “Depth visualization of ROIs is still a challenge in projecting 2D images” and cited the paper by Gavaghan et al. from 2012, which discussed the problem of parallax.¹ The parallax effect means that the apparent position of an object in relation to the background changes as the result of a change of the line of sight of the observer. It can be measured as the parallax angle, which is the angle between the different lines of sight to the object. This has been used to measure the distances of 2 objects. The parallax effect increases with the increasing distance of the object from the background or the decreasing distance from the object to the observer. If the distance of the object from the background is very small, the parallax effect is minimal. It means equally for our projection technique that the effect of parallax depends on the distance of the projected virtual image from the projection surface.

In our AR system the virtual image is projected to a surface similar to “image fusion,” and there is no measurable distance between the projected images and the projection surface, which can be the skin, skull, and brain surface.² Therefore the parallax effect does not play a relevant role in these cases. For skin incision, craniotomy, and projection on the brain surface it does not influence the planning. However, if the projection would be used for deeper structures and reliable registration is performed, the deeper structures would also function as a projection surface. The problem of projection to deep structures is more related to the image distortion, brain shift, and the registration. The parallax effect is more relevant for techniques based on head-up displays or mirror-based systems. The other point is that the line of sight of the neurosurgeon is localized in a circumscribed area, particularly after cra-

niotomy. The angle through which to look inside the head is limited by the extent of craniotomy. The neurosurgeon looks into the head in a direct line through the craniotomy approach and not from the side.

We were able to show in the study that the accuracy is similar to the navigation systems. We agree that for deep lesions the system we presented is limited, and we discussed this issue in our paper: “we believe that the described technique can be used very well to quickly and accurately guide surgery for deep brain tumors—not to project the deep tumor borders but to project the preoperatively planned approach and the craniotomy borders or any other useful information to the patient’s head, skull, or brain surface.”

2. In our opinion the measurement of the projection errors is correct, but it has limitations. We mentioned this in our paper. We are aware that a 2D image is different from the 3D reality. The aim of the study was to determine if the image projection can be used to localize the brain lesions accurately and to compare it with a navigation system. Therefore it is unavoidable to compare the 2D image with the real projection of the 2D image on the head surface. We measured the difference between the distance of the 5 fiducial markers from the tumor borders on the virtual image and the distance of the 5 fiducial markers from the tumor borders on the head phantom. The fiducial markers were the reference points. The distances between the fiducial markers were known and allowed us to measure the distance of tumor border in relation to the known distance of the fiducial markers.

With the results of the phantom study we evaluated the AR system intraoperatively and compared it with a navigation system. Prior to the surgery the MRI navigation data set was registered to the patient, showing MR images in axial, coronal, and sagittal planes with visualized tumor borders. We aimed to compare these 2 different systems directly. We compared the projected tumor borders—visualized with image projection—with the corresponding tumor borders on MRI planes.

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References

1. Gavaghan K, Oliveira-Santos T, Peterhans M, Reyes M, Kim H, Anderegg S, et al: Evaluation of a portable image overlay projector for the visualisation of surgical navigation data: phantom studies. *Int J Comput Assist Radiol Surg* 7:547–556, 2012
2. Mahvash M, Besharati Tabrizi L: A novel augmented reality system of image projection for image-guided neurosurgery. *Acta Neurochir (Wien)* 155:943–947, 2013

Trigeminal neuralgia in patients with multiple sclerosis

TO THE EDITOR: We read with great interest the report authored by Martin et al.⁵ and published in your journal (Martin S, Teo M, Suttner N: The effectiveness of percutaneous balloon compression in the treatment of trigeminal neuralgia in patients with multiple sclerosis. *J Neurosurg* 123:1507–1511, December 2015). Undoubtedly, dealing with trigeminal neuralgia (TN) in patients with multiple sclerosis (MS) still represents a controversial issue in current neurosurgical practice. Although several surgical interventions are available, we still do not have an efficient treatment method, nor do we have an agreed-upon treatment algorithm.

Currently available neurosurgical interventions to treat TN in patients with MS include percutaneous procedures such as the one highlighted by Martin et al., open surgical decompression, and stereotactic radiosurgery.^{1,5,7} Percutaneous procedures are generally favored by most neurosurgeons; however, a high recurrence rate follows these approaches, whose efficacy is still suboptimal. To improve our treatment algorithm and the outcomes of TN in patients with MS, we believe that we should keep in mind 3 important points.

First, in patients with MS who also harbor TN, the treatment should be adapted to each patient as it is critical to remember that the MS plaque is not always responsible for what we recognize as the dysfunctionality of TN and the subsequent pain. For example, Meaney et al. used MRI to study 7 patients affected by MS and TN.⁶ The purpose of their study was to investigate the underlying pathology that could contribute to patient pain. Interestingly, they found demyelinating plaque in only 1 patient. These authors concluded that even in patients with MS, the etiology of TN could be variable.

Second, if the aim of percutaneous approaches is the destruction of nerve fibers, perhaps we should consider and further investigate the method described by Bederson and Wilson and utilized by others—namely, performing a partial sensory rhizotomy of the inferior one-half to two-thirds of the sensory root of the trigeminal nerve when there is no obvious vascular compression.^{1,2} Rationally, this method allows more definitive destruction of the nerve fibers. Furthermore, it provides an opportunity to definitively rule out any vascular compression as the sensitivity of the preoperative imaging study is not absolute in terms of delineating all possible vascular abnormality that could be responsible for TN.⁸

Third, what is the exact role of local arachnoiditis and the resultant arachnoid adhesions in the pathophysiology of TN in general and in patients with MS who develop TN in particular? Arachnoiditis and thickened arachnoid adhesions during trigeminal nerve decompression surgery have been reported by several authors.^{3,4} We could speculate that MS plaque (itself an inflammatory process) could lead to local arachnoiditis, which could result in a thickened and strongly adhesive arachnoid to the trigeminal rootlets, which in turn could cause compression and changes in the local blood circulation and supply to the

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nerve. This process could play a role in generating pain in at least a subgroup of TN patients. Hence, these arachnoid adhesions may need to be released. At this time we did not have enough data regarding the significance of the observed thickened and strongly adhesive arachnoid in the pathophysiology of TN pain, although we did notice it in several surgically treated cases. Perhaps this aspect should be the subject of further investigation and research effort in the future. Regardless, we believe any arachnoid adhesions should be examined during surgery and released if they are detected. Possibly, this could be another advantage for open trigeminal nerve decompression even for patients with MS.

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References

1. Antic B, Peric P: Posterior fossa exploration in treatment of trigeminal neuralgia associated with multiple sclerosis. *Surg Neurol* **71**:419–423, 2009
2. Bederson JB, Wilson CB: Evaluation of microvascular decompression and partial sensory rhizotomy in 252 cases of trigeminal neuralgia. *J Neurosurg* **71**:359–367, 1989
3. Broggi G, Ferroli P, Franzini A, Servello D, Dones I: Microvascular decompression for trigeminal neuralgia: comments on a series of 250 cases, including 10 patients with multiple sclerosis. *J Neurol Neurosurg Psychiatry* **68**:59–64, 2000
4. Khan SA, Khan B, Khan AA, Afridi EA, Mehmood S, Muhammad G, et al: Microvascular decompression for trigeminal neuralgia. *J Ayub Med Coll Abbottabad* **27**:539–542, 2015
5. Martin S, Teo M, Suttner N: The effectiveness of percutaneous balloon compression in the treatment of trigeminal neuralgia in patients with multiple sclerosis. *J Neurosurg* **123**:1507–1511, 2015
6. Meaney JF, Watt JW, Eldridge PR, Whitehouse GH, Wells JC, Miles JB: Association between trigeminal neuralgia and multiple sclerosis: role of magnetic resonance imaging. *J Neurol Neurosurg Psychiatry* **59**:253–259, 1995
7. Sandell T, Eide PK: The effect of microvascular decompression in patients with multiple sclerosis and trigeminal neuralgia. *Neurosurgery* **67**:749–754, 2010
8. Zeng Q, Zhou Q, Liu Z, Li C, Ni S, Xue F: Preoperative detection of the neurovascular relationship in trigeminal neuralgia using three-dimensional fast imaging employing steady-state acquisition (FIESTA) and magnetic resonance angiography (MRA). *J Clin Neurosci* **20**:107–111, 2013

Disclosures

The authors report no conflict of interest.

Response

We appreciate the interest that Dr. Salma and colleagues have shown in our paper. We largely agree with each of the points raised. First, we agree entirely that TN in the context of MS is not always caused by a primary demyelinating plaque; we posit only that the plaque is a possible explanation for the increased frequency of TN in the MS population. As we stated in our paper, we accept that vascular compression and other causes of TN such as those seen in the non-MS population are still just as likely to occur in patients with MS.

Second, the surgical procedure described certainly seems to be a reasonable option; however, it is not a procedure offered at our center. And, in our experience (indeed, in the literature), we have yet to see any particular procedure proving superiority for MS-related TN.

Third, we had not considered the role of arachnoiditis in the pathogenesis of pain in MS-related TN, and it seems an interesting consideration. It would follow that an inflammatory lesion such as an MS plaque may indeed cause local inflammation and adherent arachnoid mater. We await, with interest, the findings of any such research.

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