Increasing medical student exposure to neurosurgery

TO THE EDITOR: We read with great interest the article by Lubelski et al.2 (Lubelski D, Xiao R, Mukherjee D, et al: Improving medical student recruitment to neurosurgery. J Neurosurg [epub ahead of print August 9, 2019. DOI: 10.3171/2019.5.JNS1987]). The authors discussed the decrease in the number of applicants for neurosurgery residency. The authors mentioned various strategies that can be implemented on a national level to increase the early exposure of medical students to neurosurgery in the preclinical years, and this included providing shadowing and research opportunities via the AANS mentorship program and AANS medical student chapters. We want to suggest some additional strategies that can be used to increase medical student exposure and recruitment to neurosurgery. One such strategy is to conduct local symposiums in coordination with neurosurgical interest groups (NSIG/NIG) and AANS medical student chapters wherein students residing in the same and nearby cities can attend these small sessions and learn about the different aspects and pathways in neurosurgery training. These symposiums will allow the students a chance to interact face-to-face with neurosurgeons and provide them an opportunity to connect and form meaningful relationships with neurosurgeons in different centers, and it will be especially beneficial for students in medical schools without a strong neurosurgery presence. Additionally, the formation of a subspecialty journal club with the help of interest groups wherein a medical student can work closely with a team of residents, epidemiologists, and faculty members to present an article published in a journal can aid in networking with the residents and faculty members, and in understanding the statistics as well as exposing the student to the latest developments and studies done in the field of neurosurgery.1

In their article the authors mentioned some previous studies in which it was suggested that lifestyle was a major deterrent for medical students in selecting neurosurgery as their first choice, even though the available data contradict this. In our opinion, this problem can be overcome by exposing the students to neurosurgeons who can talk about their schedule and work–life balance via online podcasts and Twitter chats, so that a broader audience can be reached and back-and-forth discussion between interested students and faculty can take place even if they are thousands of miles apart, for some studies have shown that incorporation of student feedback and an open discussion leads to an increase in the student interest in a given field. We also believe that resources like the AANS mentoring program and AANS medical student chapters, which are currently available only at a national level, should be made available on a global scale and offer membership to international medical students because this will help in increasing diversity in neurosurgical training programs and connect students all over the globe who are passionate about neurosurgery.

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References

Disclosures
The authors report no conflict of interest.

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Response
We thank Mr. Garg and Ms. Shrigiriwar for their interest and thoughtful commentary. We agree that there are numerous approaches to recruiting medical students to neurosurgery. Our survey suggested that those programs with the greatest numbers and percentage of students applying and matching in neurosurgery had active neurosur-
Surgery interest groups, research opportunities, faculty mentorship, and cadaver laboratory opportunities. Although the latter two were the most significant, all of these are interrelated. Students seek opportunities to be involved in care, have hands-on experiences, and develop relationships with mentors. Students who are involved in research collaboration tend to have close working relationships with faculty; those partaking in neurosurgery interest groups tend to do research, attend conferences, and identify mentors in the specialty.

At Johns Hopkins, we have focused on actively engaging medical students to achieve this goal. Medical students receive funding to join research laboratories between first and second year, and then are subsequently encouraged to continue research pursuits throughout medical school. Medical students with early preliminary interest are also invited to attend our daily morning educational conferences, weekly grand rounds, monthly journal club meetings, and quarterly cadaver laboratories. The faculty members actively foster these relationships and the students tend to have broad exposure to the excitement and rigors of neurosurgery. Students gain an appreciation of what is involved in neurosurgical residency, but also develop realistic expectations of the life of the neurosurgeon.

We recognize that there is more to do and that the AANS, the Young Neurosurgeons Committee, and organized neurosurgery certainly have room to improve. Although podcasts and social media communication have been exponentially growing, neurosurgery remains behind in these technologies. In recent years, however, there have been an increasing number of publications on this topic, as well as more active use of social media by the AANS, the Young Neurosurgeons Committee, and the Congress of Neurological Surgeons. Furthermore, as membership in the AANS medical student chapters and mentoring program continues to grow, there will be a natural expansion to a global level. Although international medical students and fellows often come to the US to pursue additional research and training opportunities, with increasing technology the reach can expand and collaboration can cross larger distances. Ultimately, as long as individual neurosurgeons, departments, institutions, and organized neurosurgery maintain the emphasis on engaging and recruiting medical students, the future of neurosurgery is bright.

At Johns Hopkins, we have focused on actively engaging medical students to achieve this goal. Medical students receive funding to join research laboratories between first and second year, and then are subsequently encouraged to continue research pursuits throughout medical school. Medical students with early preliminary interest are also invited to attend our daily morning educational conferences, weekly grand rounds, monthly journal club meetings, and quarterly cadaver laboratories. The faculty members actively foster these relationships and the students tend to have broad exposure to the excitement and rigors of neurosurgery. Students gain an appreciation of what is involved in neurosurgical residency, but also develop realistic expectations of the life of the neurosurgeon.

We recognize that there is more to do and that the AANS, the Young Neurosurgeons Committee, and organized neurosurgery certainly have room to improve. Although podcasts and social media communication have been exponentially growing, neurosurgery remains behind in these technologies. In recent years, however, there have been an increasing number of publications on this topic, as well as more active use of social media by the AANS, the Young Neurosurgeons Committee, and the Congress of Neurological Surgeons. Furthermore, as membership in the AANS medical student chapters and mentoring program continues to grow, there will be a natural expansion to a global level. Although international medical students and fellows often come to the US to pursue additional research and training opportunities, with increasing technology the reach can expand and collaboration can cross larger distances. Ultimately, as long as individual neurosurgeons, departments, institutions, and organized neurosurgery maintain the emphasis on engaging and recruiting medical students, the future of neurosurgery is bright.

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References

TO THE EDITOR: I read with interest the article by Yeon et al. (Yeon EK, Cho YD, Yoo DH, et al: Is 3 years adequate for tracking completely occluded coiled aneurysms? J Neurosurg [epub ahead of print August 16, 2019. DOI: 10.3171/2019.5.JNS183651]). These authors reviewed patients who had coil embolization (CE) and did not show recanalization for 36 months and reported that recanalization occurring later than 3 years after the operation is quite rare. Since long-term outcome has been a concerning issue after CE, the results reported by Yeon et al. are important to reduce anxiety and unnecessary medical costs for checkups in patients with treated aneurysms. However, I have several questions regarding this work.

Previous studies concerning recanalization after CE have found aneurysm size to be a major risk factor, but Yeon et al.’s results differed from already existing results. Though aneurysms larger than 10 mm were found in only 4% of Yeon et al.’s patient cohort, recanalization occurred only in the aneurysms smaller than 10 mm. This may have occurred because many large aneurysms might have recanalized before 36 months and were excluded from the analysis, or because of patients who could not be followed up for some reason. Because this result is the opposite of what has been demonstrated in previous studies, the report by Yeon et al. would have been improved by the presentation of an interpretation of these findings.

Three years seems adequate for tracking particular aneurysms after coil embolization

TO THE EDITOR: I read with interest the article by Yeon et al. (Yeon EK, Cho YD, Yoo DH, et al: Is 3 years adequate for tracking completely occluded coiled aneurysms? J Neurosurg [epub ahead of print August 16, 2019. DOI: 10.3171/2019.5.JNS183651]). These authors reviewed patients who had coil embolization (CE) and did not show recanalization for 36 months and reported that recanalization occurring later than 3 years after the operation is quite rare. Since long-term outcome has been a concerning issue after CE, the results reported by Yeon et al. are important to reduce anxiety and unnecessary medical costs for checkups in patients with treated aneurysms. However, I have several questions regarding this work.

Previous studies concerning recanalization after CE have found aneurysm size to be a major risk factor, but Yeon et al.’s results differed from already existing results. Though aneurysms larger than 10 mm were found in only 4% of Yeon et al.’s patient cohort, recanalization occurred only in the aneurysms smaller than 10 mm. This may have occurred because many large aneurysms might have recanalized before 36 months and were excluded from the analysis, or because of patients who could not be followed up for some reason. Because this result is the opposite of what has been demonstrated in previous studies, the report by Yeon et al. would have been improved by the presentation of an interpretation of these findings.
In the study by Yeon et al., 4 of the treated aneurysms that recanalized (80%) were of the sidewall type. Many interventionists say that sidewall-type aneurysms are most suitable for CE because, with laminar flow by the coil-thrombus complex, a neointima is formed that isolates the abnormal aneurysm wall from the lumen, which attains cure of the aneurysm. It may be because of the small event number (n = 5) of recanalization cases in Yeon et al.’s study that these results are also the opposite of what has been widely reported.

Yeon et al. calculated the recanalization rate by using the person-year method and calculated the rupture rate of unruptured cerebral aneurysms (UCAs) using the following formula: (number of events)/(number of patients × observation period). It is well known that small UCAs harbor a smaller bleeding risk than larger aneurysms, and the rupture risk varies for different aneurysm locations. If the cohort consists of many patients with low-rupture risk aneurysms, the rupture rate becomes small because the denominator (the observation period) becomes large. For example, paracclinoid aneurysms rarely bleed, though they are treated aggressively by CE. It is not clear whether ruptures from UCAs and those from recanalizations from coiled aneurysms behave similarly, but it would be appropriate to assume most paracclinoid aneurysms are stable and will rarely recanalize after CE. In their reported study, Yeon et al. divided the aneurysms into anterior and posterior circulation aneurysms, but in another article from their institution, Choi et al. reported that 37.0% of their cohort was made up of patients with ICA aneurysms, most of which should presumably have been paracclinoid or internal carotid–superior hypophyseal artery aneurysms. In addition, Yeon et al. reported that 62.3% (208 aneurysms) were small aneurysms equal to or smaller than 5 mm, and 57 aneurysms were ruptured, which means that the majority of treated aneurysms were UCAs with small rupture risk. So, we have to pay attention to the bias for the analyzed aneurysms in this cohort.

With good management, only 5 patients reported by Yeon et al. showed recanalization during the study period. The authors calculated the hazard ratio by multivariate regression analysis using Firth’s method to compensate for their small event number, and prior retreatment was a statistically significant risk factor for late recanalization. Unfortunately, I do not know how powerful Firth’s method is, but the number of recanalizations, 5, means that among them, at least 3 aneurysms which recanalized were sidewall type “and” ruptured, and at least 2 were initial “and” unruptured, and so on. Thus, considering the small number of events, multivariate analysis does not seem to produce meaningful values.

The conclusion derived from the results of Yeon et al. should be that most small aneurysms, including paracclinoid ones, rarely recanalize if they do not recanalize within 3 years after CE. As the authors stated, prospective multicenter observational study is needed, but the cohort should be large enough to withstand stratification by ruptured/unruptured status, size, and so on.

Finally, I appreciate the authors’ focus on long-term outcome, which was left to be determined, thus leading to further studies for understanding the prognosis after CE.

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Disclosures
The author reports no conflict of interest.

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Response
We would like to thank Dr. Kimura for his interest in our paper. Our study pertained to long-term durability during follow-up of coiled aneurysms completely occluded at 3 years (in order to determine how long we should keep track of patients with coiled aneurysms) and did not address general risk factors for recanalization of coiled aneurysms.

In this series, delayed recanalization was confined to aneurysms smaller than 10 mm. As Dr. Kimura notes, large-sized aneurysms tended to recanalize in less than 36 months, precluding this analysis. The same was true of various attributes, such as type of aneurysm (sidewall vs bifurcation), location (anterior vs posterior circulation), neck width (narrow vs wide), and presentation (unruptured intracranial aneurysm vs subarachnoid hemorrhage). Hence, stable occlusion at 3 years in otherwise precarious situations (large, bifurcation, posterior, wide-necked, or ruptured aneurysms) implies exceptional durability.

We also agree with Dr. Kimura’s comments on the limitations of this study, namely the few instances of delayed recanalization, the rather low representation of ruptured or large aneurysms, and the lack of consistency in modality and interval of follow-up. As elaborated in the Discussion section of our article, such failings are inherent in retrospective reviews and seemingly reflect real practice situations. More conclusive support is clearly needed, acquired through large observational studies and prospectively collected data.

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Propionibacterium acnes and aseptic bone graft resorption

TO THE EDITOR: We would like to make many comments on an article by Butenschoen et al. (Butenschoen VM, Seifert M, Meyer B, et al: Presence of Propionibacterium acnes in patients with aseptic bone graft resorption after cranioplasty: preliminary evidence for low-grade infection. J Neurosurg [epub ahead of print August 30, 2019. DOI: 10.3171/2019.5.JNS191200]). In this paper the authors demonstrate that aseptic bone resorption may be caused by low-grade infections with Cutibacterium acnes (formerly Propionibacterium acnes). Cutibacterium acnes (P. acnes) is a part of normal human microbiota, and this microorganism is difficult to eradicate with simple skin preparation. It has been associated with infection of many devices used in neurosurgery (external ventricular drains, shunts, and cranioplasty mesh) and an infection rate up to 38%. In recent years the relevance of P. acnes as a cause of postneurosurgical infection has been recognized. In addition to the detailed analysis presented by the authors, we would like to emphasize that, although the authors mention that “autologous bone graft reimplantation remains the standard treatment after decompressive craniectomy,” this is a matter of debate. Despite being an accepted practice in many neurosurgical centers, it does not mean that it is the standard treatment. Despite its greater applicability, the evidence for management and performance of a cranioplasty with autologous grafting is scarce in the literature. The concept of standard of care that includes both content and quality is difficult to implement due to lack of information.

Another interesting point to note is that patients with traumatic brain injury (TBI, 31%) and subarachnoid hemorrhage (SAH, 13%) accounted for 44% of those with subsequent septic bone infections. It would be interesting to know the premorbid condition of these patients (diabetes, primary immunosuppression, or associated with the use of corticosteroids). TBI and SAH are associated with systemic inflammatory phenomena that may be associated with alteration of the immunological system. In other words, these patients may be at greater risk of developing bone flap infections. Can we make this as a case to propose cranioplasty with heterologous graft from the beginning in this subgroup of cases?

The authors should be congratulated for this very interesting study, given the significant number of patients who develop flap infection by C. acnes. We believe that institutional strategies for prevention and early detection should be established, such as a skin swab in high-risk patients. There is an urgent need for clinical management guidelines as an effort of the international neurosurgical community to establish the best management options for cranioplasty in patients who have had a craniectomy.

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Disclosures
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Response
We much appreciate the interest in our article. We thank the authors for their letter to the editor and are delighted to have the opportunity to respond to several topics and questions raised.

First, we would like to address the issue of the “standard treatment after decompressive craniectomy.” In our department, the gold standard remains the reimplantation of the autologous skull after removal for decompressive treatment. Despite their complications, alloplastic material is only used in exceptional cases such as infection of the skull bone, aseptic bone resorption, TBI with fragmented skull, or chronic wound healing disorders with the need of a flatter cranioplasty. The indication for a computer-aided–design cranioplasty is therefore, at least in our department, limited to cases in which the autologous bone graft cannot be reimplanted. Yet, Moscote-Salazar et al. are right. The approaches of cranioplasty after decompressive craniectomy are different between countries and departments alike, and within the last 10 years the availability of various alloplastic materials for cranioplasty has led to approaches favoring primary alloplastic cranioplasty in some depart-
ments. One large multicentric study investigating the pros and cons of this matter is currently ongoing in our country. Regarding the overall risk of bone resorption (by its very definition only existing in autologous bone grafts), the material used for cranioplasty is indeed a matter of debate, and is why the causes of reoperations due to bone resorption need to be investigated—which was one of our aims in our study.

Second, Moscote-Salazar et al. point out that 44% of the patients with subsequent septic bone infections initially underwent operation for TBI and SAH. In our retrospective data, there was no significant difference in comorbidities in patients with TBI or, for example, meningioma. In fact, patients with TBI had a similar age compared to those with meningioma (mean age 46 years vs 48 years, respectively). As mentioned, corticosteroid treatment would definitively be considered a risk factor for bone infection and wound healing disorders if administered on a long-term basis preoperatively. In our patients, however, corticosteroid therapy was not applied in any patient after TBI or after SAH. Therefore, we do not see any confounding factors regarding the success of autologous cranioplasty.

We do agree on the importance of detection and therefore the possibility of further future prevention of bone resorption, because it impacts the success rate of autologous bone graft cranioplasty. Up to now, we can only emphasize the importance of microbiological analysis and, if possible, sonication analysis of the bone graft in cases of suspected resorption because it may change the preoperative single-shot antibiotic at the time of cranioplasty. It is important to note that Propionibacterium acnes builds a biofilm, and is therefore not only difficult to eradicate, but can also be more resistant to preoperative prophylactic antibiotics such as clindamycin, with the need of further intravenous treatment.

Evaluating whether biopsy and consecutive targeted long-term antibiotic treatment before revision surgery in cases with bone resorption lowers the complication rate of these surgeries might be a good target for a future trial. Propionibacterium acnes may be one of the pathogens leading to “aseptic” bone resorption, and more information on its presence and treatment needs to be acquired in order to define its role in patients undergoing cranioplasty after decompressive hemicraniectomy.

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Random assignment of patients to intraoperative neuromonitoring for unruptured intracranial aneurysms?

TO THE EDITOR: We read with interest the study by Greve et al., in which they compared neurological outcomes of patients with intraoperative neuromonitoring (IONM: somatosensory evoked potentials [SSEPs] and motor evoked potentials [MEPs]) to a historical control without IONM (Greve T, Stoecklein VM, Dorn F, et al. Introduction of intraoperative neuromonitoring does not necessarily improve overall long-term outcome in elective aneurysm clipping. J Neurosurg. 2020;132[4]:1188–1196). No difference was observed for clipping of unruptured intracranial aneurysms. The authors state, “Hence, the ethical burden to perform randomized controlled trials with and without the use of [IONM] in [elective microsurgical clipping of unruptured intracranial aneurysms] might by overcome.”

Clinical equipoise, “genuine uncertainty within the expert medical community,” should be informed by our certainty in the results of studies. In their nonrandomized comparative study, the authors did not account for differences in prognostic variables between patients that could also have predicted the use of IONM. This typically requires multivariate methods (regression, propensity analysis) or stratification of effects. In fact, patients in the IONM group were older than those in the no-IONM group, and age was correlated with worse postoperative outcomes. Confounding may have resulted in no observed difference when there was a true association between IONM and outcomes. Accounting for confounding in nonrandomized studies is a basic requirement before results can be accepted with confidence.

As the authors acknowledged, a limitation of their study is the small sample size. Assuming a 10% risk of new neurological deficit and that IONM would cut this in half, 435 procedures in the IONM and no-IONM groups (870 total) would be required for a conventional 80% power (Pearson’s chi-square test). The authors reported results on 138 procedures with IONM and 136 procedures.
without IONM. Their underpowered study (power = 27%) may have missed an IONM effect on outcomes if one was present.

In the absence of randomized studies, 2 other comparative studies of IONM for middle cerebral artery (MCA) aneurysms might be given more weight in informing medical opinion. Both Byoun et al.3 (SSEPs for unruptured MCA aneurysms) and Yue et al.6 (MEPs for MCA aneurysms, 72% ruptured) used multivariate regression to account for confounding. Contrary to the results reported by Greve et al., both studies reported improved postoperative outcomes for IONM compared with historical cohorts without IONM.

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References

Disclosures
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Response
We appreciate the authors’ valuable discussion of statistical methods, which highlights important aspects of IONM and which we actually addressed in our study. The authors discuss the age difference between the IONM and no-IONM cohort. We stressed that although this difference was significant, the absolute magnitude was low (3 years of median difference), and thus, a potential confounding effect is limited. Of note, all other demographics were similar between groups. Large IONM studies are sparse, and part of the significance of our study was the prospect to set up future trials where IONM and no-IONM cohorts are compared in a truly prospective manner.

Although we reported on 2 large cohorts of aneurysm patients, the sample size did not allow us to apply binary logistic regression modeling, which was explicitly mentioned as a limitation. We therefore discussed numbers needed to treat as the parameter of choice to describe differences in both groups. We agree with the authors that future prospective IONM studies will require large sample sizes in both treatment arms to achieve clinical significance, as long-term results may not differ significantly between the two groups, a conclusion also reached in a paper cited by the authors.2

Furthermore, the authors referred to another study1 in which 411 clipping procedures were analyzed. This study only included SSEP monitoring, which has been deemed insufficient by other groups to detect cortical and subcortical ischemia when used without MEP monitoring.3–5 Nevertheless, the authors found that SSEP monitoring is independently associated with a reduced rate of ischemia detected on postoperative imaging. It should be noted that the authors could not detect any difference in postoperative neurological outcome, objectified by the modified Rankin Scale score at early and late postoperative time points, which does not refute but rather confirms our results.

The authors draw attention to a study in which 89 patients were included and divided into two groups of 45 and 44 patients each.2 Of note, this study did not aim exclusively at elective cases like our data but included 64 of 89 ruptured aneurysms. Surprisingly, subarachnoid hemorrhage, preoperative Glasgow Coma Scale score, and motor status were not significant risk factors for the functional long-term outcome, while MEP application was significant only after adjustment for confounding factors in a second multivariate model. The authors admitted that they struggled with a sample size that was too small to apply logistic regression models with statistical confidence. In addition, they reported that randomization was not ideal, as they “inclined to proceed with MEP monitoring for the assumed benefit,” which makes selection bias very likely.

In contrast, our study included a larger sample size of exclusively elective cases, but we still refrained from logistic regression modeling to avoid exactly this kind of bias.

In conclusion, we are confident that our study provides additional evidence that large, prospective cohort trials with prior sample size estimation and a rigorous study protocol are both necessary and ethically justifiable to obtain definitive evidence on the efficacy of IOM during clipping of intracranial aneurysms.

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References
Awake craniotomy and transcortical MEP monitoring for resection of precentral gliomas

TO THE EDITOR: It was with great interest that we read the article by Saito et al.1 about the combined usage of awake craniotomy and transcortical motor evoked potential (MEP) monitoring for the resection of precentral gliomas (Saito T, Muragaki Y, Tamura M, et al. Awake craniotomy with transcortical motor evoked potential monitoring for resection of gliomas in the precentral gyrus: utility for predicting motor function. J Neurosurg. 2020;132[4]:987–997). We agree, to a great extent, with the usefulness of intraoperative MEP monitoring combined with awake craniotomy when resecting these gliomas. However, we wish to comment on two issues.

1) The combined findings of MEPs (decline > 50%) along with involuntary movements (IVMs) do not always correlate with an intraoperative decline in motor function and vice versa. We strongly believe that it is the point of decline in motor function that is highly correlated with determining the progression of surgery, rather than relying on MEPs, although combined usage is always recommended. How did the authors correlate these two aspects intraoperatively, rather than analyzing the motor deficit 6 months later? A decline in motor function per se for each operation, even with or without any change in MEPs, is a powerful indicator in deciding whether to proceed with resection or not.

2) In financially disadvantaged countries, which lack even basic intraoperative monitoring (IOM) devices, we are still greatly in favor of awake craniotomies in which the operative team evaluates intraoperative motor function, and there are verbal responses in cases of precentral tumors. The simple lack of IOM devices should not deter a surgeon from performing such surgeries.

We await with great enthusiasm further studies on the comparative usage of awake craniotomies with and without IOM devices in such cases of gliomas.

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Disclosures
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Response
We thank Dr. Ansari for his interest in our work. We would like to respond to the two issues he raised.

First, he mentioned that the findings of an MEP response do not always correlate with IVMs. Furthermore, monitoring of IVMs is a powerful indicator of motor function and highly sensitive with few false-negative cases in motor function. However, in our experience, monitoring of IVMs may sometimes show false-positive responses in actual motor function, due to removal of a tumor causing physical compression or insufficient awakening. Actually, of 22 patients with a decline in IVMs, 11 patients showed a decline in MEPs ≤ 50%, and only 2 of these 11 patients had mild motor deficits 6 months after surgery, which did not affect daily life. In contrast, 11 of 22 patients with a decline in IVMs showed a decline in MEPs > 50%. Of these 11 patients, 8 (73%) had motor dysfunction 6 months after surgery, including 2 patients with moderate deficits and 1 patient with severe deficits. Therefore, we believe that the combination of these two factors is useful when resecting gliomas in the precentral gyrus and for predicting postoperative motor function. Consequently, we recommend cessation of further tumor removal if a patient shows a decline in both IVMs and MEPs (> 50%).

Second, unfortunately, we have no experience in performing awake craniotomy in patients with a precentral gyrus tumor without an intraoperative monitoring IOM device. The advantage of awake craniotomy with neurophysiological monitoring when resecting gliomas is that the surgeon is able to observe the correlation between the results of MEP monitoring and IVMs.1 As we mentioned above, monitoring of IVMs may sometimes show a false-positive result in actual motor function. Therefore, there is a risk of minimal tumor removal if surgery is performed only by monitoring IVMs. Thus, we believe that the robustness of motor functional monitoring can be improved by combining an awake craniotomy with neurophysiological...
clical monitoring during removal of gliomas in the precentral gyrus.

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Intraoperative neuromonitoring in elective aneurysm clipping: methodology matters


This article is important, as it is one of the few comparative reports describing neurological outcomes with and without intraoperative neuromonitoring IONM use in elective microsurgical clipping of unruptured intracranial aneurysms (ECUIAs). Interestingly, the authors found that there was no positive impact from introducing somatosensory evoked potential/motor evoked potential (SSEP/MEP) monitoring on overall neurological outcome, which is in contrast with previous studies.2,3 Most articles support the positive effect of multimodal IONM with SSEP and MEP by transcranial electrical stimulation (TES) but also by direct cortical stimulation (DCS), which seems to overcome the limitations of each individual procedure with better results but was not used in the present study.2–5

The authors applied a personalized protocol in which MEPs were elicited by TES, and the chosen montages were C3/C4, C3/Cz, or C4/Cz for upper extremities and C1/C2 for lower extremities. The use of C3/C4 could be a challenge, as muscle responses were very likely elicited by the excitation of the corticospinal tract being very distal from the cortex. Moreover, MEPs elicited by TES—even with the lowest stimulation and the most focal montages—are always of concern because 1) there is no clinical evidence about how superficial the stimulation site is, 2) current may spread deeply in the white matter, and 3) muscle contractions may interfere with surgery. Therefore, in order to provide more focal stimulation and to allow continuous monitoring without patient movement, DCS should be used.4–7

It is remarkable that, despite the authors’ maintaining that cortical ischemia can be readily detected by SSEP monitoring, it has been previously shown that the combination of SSEPs and MEPs with TES and DCS improves the outcome after aneurysm surgery.4,5,7 Ischemic changes missed by SSEPs may be detected by MEPs, and vice versa.3,8 The lack of MEPs elicited by DCS in Greve and colleagues’ study may have influenced and compromised the results, and their false-negative results may have arisen from deeper stimulation bypassing ischemic structures.

Furthermore, the authors report the use of inhalational and thiopental anesthetic agents, which could be a confounding factor, increasing motor threshold and therefore deep structure activation and thus bypassing brain tissue with imminent ischemia. Therefore, this anesthetic context might lead to an incorrect interpretation of results and, as has been largely recommended, the most sensitive and reliable anesthetic regimen for IONM is total intravenous anesthesia.9,10

The present letter intends to highlight how the use of DCS combined with the proper TES montage and also SSEPs has emerged as the most efficient way to achieve optimal effect of monitoring on clinical outcome in aneurysm surgery. In addition, a suitable intravenous anesthesia protocol has to be carefully selected. Hence, we have to point out that the study has limitations as far as usefulness of neuromonitoring is concerned. This question can only be answered with a study using DCS and total intravenous anesthesia.

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Response

We appreciate the authors’ interesting letter in response to our study, shedding light on important aspects of monitoring literature in neurosurgical research. We agree that the topic of our study is relevant because there is still an urgent need for comparative studies on patients undergoing ECUIA with and without IONM.

The application of new technologies in the operating room should solely be justified when studies with a high level of evidence show improved outcome. However, large randomized studies in neurosurgery are scarce, especially in the field of IONM, and studies before and after the introduction of new IONM methods might in part fill this gap.

The authors claim that our study found no positive impact and thus stands in contrast to previous literature. However, we explicitly discussed a subtle trend toward a positive clinical impact and thus stands in contrast to previous literature. This difference is often disregarded, and the high sensitivity of IONM is somehow equated with favorable patient outcome. Furthermore, the authors discuss that a suboptimal montage setup and the lack of DCS could possibly compromise IONM results. While our technical setup is mostly in line with those of other groups and our results on sensitivity and specificity largely overlap with the literature, we tried to carefully discuss general technical limitations and stressed the importance of protocol improvements in the future.

While we are grateful for the authors’ discussion of DCS, we would like to refer to the study by Deletis et al., where they showed that by using close-to-motor-threshold stimulation and a focal stimulating montage, TES and DCS do not differ significantly in their ability to detect motor cortex or pathway lesions. More importantly, a reported 3% complication rate for DCS might itself represent a risk factor for impaired clinical outcome. We therefore encourage conducting prospective clinical trials on the topic of outcome measurement with and without DCS.

In conclusion, we strongly advise in favor of controlled prospective and comparative trials for IONM in the setting of ECUIA.

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Disclosures
The authors report no conflict of interest.

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References
How to define tremor recurrence after TcMRgFUS treatment?

TO THE EDITOR: We read with interest about the usefulness of relative fractional anisotropy in the targeted ventral intermediate nucleus for the prediction of symptomatic improvement at the 1-year follow-up after transcranial MR-guided focused ultrasound (TcMRgFUS) thalamotomy for essential tremor by Hori et al.1 (Hori H, Yamaguchi T, Konishi Y, et al. Correlation between fractional anisotropy changes in the targeted ventral intermediate nucleus and clinical outcome after transcranial MR-guided focused ultrasound thalamotomy for essential tremor: results of a pilot study. J Neurosurg. 2020;132(2):568–573). We are delighted to see such significant work.

However, we have some questions about the definition of recurrence in the paper. According to their citations,2–5 the improvement ratio should be calculated according to the following formula: (baseline score – follow-up)/baseline score, which indicates that a higher improvement ratio means better tremor control. However, in the paper, the Clinical Rating Scale for Tremor (CRST) improvement ratio at 1 year after TcMRgFUS thalamotomy for essential tremor (0.61 ± 0.12) was higher than that of the improvement group (0.61 ± 0.12). It appears that the recurrence group defined in the paper actually experienced better tremor relief according to the formula. The authors might have used another formula to calculate the improvement ratio; we hope they can clarify the formula that they used to calculate the improvement ratio.

In addition, how did you define if the patients experienced recurrence in the paper? We know that improvement ratio is a continuous variable; is there a clear cut-off value to define recurrence? Which score, hand tremor score or the CRST total score, should we use to define the recurrence? We hope the authors can help us answer these questions.

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References

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The authors report no conflict of interest.

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Response
We are thankful to colleagues from Beijing for their interest in our work. They have raised very important issues on the appropriate assessment of tremor and the diagnosis of its recurrence after TcMRgFUS thalamotomy (or any other treatment). The answers to these questions are not as simple as they may seem.

The CRST is a well-established instrument for evaluation of patients both before and after therapy. In our study, tremor in the treated hand was assessed using CRST part A (the hand tremor with rest, posture, and action/intention) and part B (5 tasks of handwriting, drawings, and pouring), which seems quite reasonable considering the therapeutic objectives. The CRST improvement ratio was calculated by normalizing the CRST score at 1 year after TcMRgFUS thalamotomy to those before treatment as a fold change (follow-up score/baseline score); thus, larger values indicated worse response to treatment. Application of such a method excludes the sign before the value, which may simplify the interpretation of results. Nevertheless, the CRST improvement ratio is often assessed as a relative change expressed in percentage (follow-up score – baseline score)/baseline score × 100%. Obviously, both aforementioned parameters perfectly correlate with each other. In our series, the CRST improvement ratio at 1 year after treatment varied from 0.5 to 1.12 (mean 0.74 ± 0.22, median 0.71) and the relative CRST improvement ratio from −50% to +12% (mean −26% ± 19%, median −29%).

All patients in our series demonstrated more or less...
prominent symptomatic improvement immediately after TcMRgFUS thalamotomy (1 nonresponder was excluded from the analysis), but some of them noted tremor recurrence thereafter. Here is the problem: how should the appropriate diagnosis be made? It is doubtful that we can establish some standard cutoff value of the CRST score that can be effectively applied in each individual case to define clinical deterioration. The magnitude of symptoms both at baseline and at relapse may vary, and they may have different impacts on the quality of life. Thus, how should this be considered if a uniform cutoff value of the standard scale is used? The time interval to relapse may differ from one case to another; how can we adjust to this variability and should we perform a comparison of the CSRT score at recurrence to those at baseline, or at the time of best response to treatment? At present there are no clear answers to these questions. Therefore, with regard to tremor recurrence, we are favoring decision-making based on the thorough neurological examination of patients by highly experienced colleagues specialized in movement disorders, with application of the CRST (and some other scales) only as a useful adjunct to reasonable clinical judgment.

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