Navigated transcranial magnetic stimulation: another tool for preoperative planning for patients with motor-eloquent brain tumors

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Dr Frey and his group are to be congratulated on the successful demonstration of the use of navigated transcranial magnetic stimulation (nTMS) as an aid in the resection of brain tumors in motor-eloquent locations. They correctly state that one of the dilemmas of brain tumor surgery in eloquent cortex is how to gain benefit for the patient in terms of extended survival, maintenance or even improvement of function, and quality of life while at the same time not risking new neurological deficits. The authors point out that the natural history of the disease must be weighed against the risk generated by the intervention itself. This is especially true in the realm of low-grade gliomas, where the natural history can be relatively benign, but postoperative complications can have great impact on the patient's overall outcome. On the other hand, there is a body of emerging literature that indicates that the extent of resection of a given glioma is positively correlated with patient survival. When counseling patients on the best course of action in the preoperative setting, one must walk a delicate balance between aggressive treatment and the potential for complications. Thus, any tool that allows for preoperative assessment of critical brain function in relationship to the location of a given lesion is highly valuable. The authors of this paper observe that there is an inherent problem with preoperative tests that “lead to improper restraint in surgical indication” and thus undertreat a given patient.

In this study, the authors compared 2 groups: patients treated over 2 years without nTMS and patients treated over a subsequent 5 years with nTMS. Unfortunately, this study design complicates interpretation, as the authors have certainly improved their technique and judgment during these time frames. Nevertheless, there are some solid findings from this study. First, this report confirms that nTMS is well tolerated by patients without any induced seizure activity. The authors also report increased extent of resection and fewer biopsy-only cases in the nTMS group. Progression-free survival (PFS) was improved but overall survival (OS) remained unchanged. The improved PFS might be explained in part by a much lower number of “biopsy-only” cases. We also are unaware of the mix of patient molecular profiles between the 2 groups (methylguanine methyltransferase promoter methylation, isodehydrogenase-1 mutation, 1p19q deletion, etc), which could impact PFS or OS. It is also important to note that measurement of PFS in gliomas can be technically problematic given the reliance on imaging and the timing of imaging as well as definitions of “progression.” Nevertheless, PFS is used more and more frequently in clinical trials to evaluate outcomes for patients with gliomas. Therefore, the improved PFS in the nTMS group is even more impressive when one considers that it was achieved without an increase in neurological complications.

Another of the limitations of this technique not mentioned in the paper is that nTMS is still subject to interpretation by the surgeon preoperatively. A similar preoperative imaging modality, functional MRI (fMRI), suffers from the same limitations. I routinely use fMRI in a manner similar to that described in this paper to help guide decision making and counseling of patients with tumors located in presumed motor cortex; however, I have never felt comfortable relying solely on the preoperative fMRI. I use the fMRI data as a starting template as I begin intraoperative cortical stimulation. Dr Frey and his group used intraoperative motor cortical stimulation in a similar manner to confirm their nTMS findings. They found that the mean (range) distance between nTMS and intraoperative stimulating mapping hot spots for abductor pollicis brevis was 6.2 mm (0.4–14.8). This is a very nice correlation between the 2 methods; however, it has been demonstrated that injury to neurological pathways occurs when tumor resection is carried out within a distance of 5–10 mm from the stimulation positive site. This would imply that nTMS alone may not be sufficient for determining a safe surgical corridor. Along these same lines, the authors observe that the use of phase reversal determination was waived in 95% of cases, allowing for smaller craniotomies in 17.5%. Once again, I routinely use phase reversal measurement in motor mapping cases. The fMRI can be helpful in determining where to lay down the leads for initial phase reversal determination. The nTMS could potentially eliminate this step, although that is rarely a complicated or prolonged exercise in the operating room. I am not sure that the phase reversal leads are the determining factors in fashioning the craniotomy size. Therefore, nTMS may not change this aspect of my practice. Furthermore, this technique is limited to motor function and is not useful for speech or language mapping, thus the need for preoperative fMRI or intraoperative mapping remains.

As mentioned above, the major limitation of this study is the comparison of 2 cohorts with data not collected concurrently.
The authors believe that a randomized study would not be feasible or ethical, since “a randomized study would deny many patients the best available treatment and in our opinion would contradict the ethical commitment of a physician”; however, one could easily question whether nTMS is the “best available treatment.” Wouldn’t a trial where half of the patients received an fMRI and/or magnetic source imaging using magnetoencephalography randomized against patients treated using nTMS be a reasonable option? A number of studies have compared fMRI and intraoperative cortical mapping in this way, so this might be a comparable control group.5,6

As a neuro-oncological surgeon, I applaud any attempt to improve surgical therapy for glioma; however, I am acutely aware that it is ultimately the better understanding of the inherent biology and development of treatments aimed at reversing the aggressive and infiltrative nature of these tumors that will lead to a cure for these patients. The techniques described in this paper will improve surgical therapy, but I think the authors overstate the importance of nTMS when they conclude: “The impact of this study should go beyond the neurosurgical community, since it could fundamentally improve treatment and outcome and its results will likely change clinical practice.” Navigated TMS is a wonderful new tool to add to the current tools we have available for glioma surgery, including fMRI, magnetoencephalography/magnetic source imaging, intraoperative cortical mapping and monitoring, neuronavigation, and intraoperative MRI.

References