Intraoperative magnetic resonance spectroscopy and gliomas

AMMAR SHAIKHOUNI, M.D., PH.D., 1 AND E. ANTONIO CHIOCCA, M.D., PH.D. 1, 2

1Department of Neurological Surgery, James Cancer Center and Wexner Medical Center at The Ohio State University, Columbus, Ohio; and 2Department of Neurosurgery, Brigham and Women’s Faulkner Hospital, Boston, Massachusetts

Surgery plays an instrumental part of the diagnosis and management of gliomas. While there is no Class I evidence showing that extent of resection improves survival, there is evidence that shows correlation between extent of resection of the tumor and increased survival in patients with glioma. 6 Today, most neurosurgeons agree that one of the goals of glioma surgery should be maximum safe resection of the tumor. Intraoperative MRI (ioMRI) was developed to help reach this goal. Although there is still no Class I evidence showing that the use of ioMRI leads to increased survival of patients with glioma, 1 a recent trial shows that the use of ioMRI leads to a more extensive resection when compared with resection done without utilization of this technology. 7 Early ioMRI utilized low magnetic field strengths (<0.5 T). More recently, high-field ioMRI (1.5 T or 3.0 T in strength) has been deployed in a number of centers. In comparison with low-field ioMRI machines, these high-field ioMRI machines are more expensive, require more resources to operate, and pose significant safety challenges in the operating room. As a tradeoff, they produce more precise images and reduce the scanning time. Because of these properties, they allow the use of other valuable sequences, such as diffusion-weighted imaging (DWI) and magnetic resonance spectroscopy (MRS). These sequences have been widely utilized in the diagnosis and follow-up of gliomas to help differentiate them from other lesions with similar MRI characteristics.

Magnetic resonance spectroscopy uses a few known histochemical properties of brain tumors. It generates a chemical spectrum of a region of interest with a prominent spectral peak that helps identify the nature of the tissue in that region. The N-acetyl-aspartate (NAA) signal is usually decreased in tumors signifying death of normal neuron. On the other hand, the choline (Cho) signal peak is increased, signifying rapid membrane turnover. To identify regions with tumor, the ratio of two signals is used, and a threshold is typically utilized to delineate tumor from other lesions. This method has been used to help differentiate brain tumors from other lesions with similar MRI appearance. 2 However, less is known about its efficacy in intraoperative guidance for glioma resection.

In the current article, 5 Pamir et al. expand the description of their experience with high-field ioMRI, initially described in their 2010 article. 4 In both studies they limited the analysis to surgeries for low-grade glioma (LGG). The reader is advised to read the two papers together to better understand the approach utilized by the authors. In their previous study, they showed that the use of ioMRI lead to a 32% increase in surgeries with a gross-total resection. They also reported using single-voxel ioMRS with a threshold Cho/NAA ratio to differentiate residual tumor and surgical changes when residual T2 hyperintensity was left at the resection margin. In 12 of 21 cases, the MRS characteristics were consistent with tumor at this margin, and further resection was performed. In the remaining 9 cases, the MRS characteristics were more compatible with operative changes and thus no further resection was attempted. Therefore, this study could not address whether the residual area of T2 hyperintensity was indeed not neoplastic in the cases not selected for further resection.

In the current report, the authors attempt to address this issue and define how many patients with residual T2 changes in the resection cavity and MRS signal characteristics suggestive of tumor truly had tumor by using a multi-voxel approach. They correlated the MRS signal in 20 voxels of interest (VOIs) in 14 patients with residual T2 hyperintensity at the resection margin with the final histopathological diagnosis from the tissue that corresponded to those same voxels. They reported that 14 of the 20 VOIs contained tumor on final pathology (70%). Intraoperative MRS was 85.7% sensitive and 100% specific in diagnosing tumor pathology. Therefore, MRS of the T2 hyperintensity of the resection cavity possessed a 100% positive predictive value and a 75% negative predictive value for tumor. They concluded that ioMRS is a useful adjunct to standard intraoperative imaging protocols in deciding if an abnormal area on T2-weighted images is still tumor.

The authors should be highly congratulated for the design of this study, which is the first to provide a quantitative analysis, as measured by sensitivity and specificity, for the use of MRS in diagnosing residual tumor. These results encourage further exploration of different imaging sequences or paradigms in the intraoperative analyses of tumors. 4, 5 The results also provide a new use for MRS in
addition to its previously described capacity for differentiating between recurrent tumor and radiation changes, where MRS was found to be 85% sensitive and 69% specific for tumor recurrence.\(^8\)

The study suffers from a few limitations. The sample size is small, which is expected given that the data are from a single center and were collected over a relatively short period. It is not clear what criteria were used to select patients for ioMRI- and ioMRS-guided resection. This important information would be beneficial for interpreting the positive and negative predictive values, as these rely on the prevalence of disease. The authors present data on the diagnostic accuracy of intraoperative DWI (ioDWI) but it seems as if the data were not utilized to guide surgical decision making. One wonders if inclusion of the ioDWI in a larger decision model using pattern recognition technology could yield a better prediction tool to guide resection.\(^2\) This may be a topic that could be addressed in future work.

The authors present a strong case for the use of high-field magnets intraoperatively as low-field magnets do not possess the signal-to-noise ratios that would lead to reliable MRS. One of the weaknesses of the ioMRS, which the authors acknowledge, is its low negative predictive value. Indeed, some neurosurgeons will favor resection of suspicious lesions from safe areas rather than risk leaving behind tumor. Furthermore, since T2 hyperintensity represents either residual tumor or tissue affected by surgical changes, one can argue that the tissue may already be nonviable and thus its resection is unlikely to lead to more damage. Clearly, this argument would be fallacious if these areas of T2 hyperintensity were in eloquent cortex. Furthermore, utilizing a very low-field strength ioMRI, T1-weighted gadolinium-enhanced or T2-weighted ioMRI sequences were shown to possess a sensitivity of 82% and specificity of 95% in diagnosing tumor versus normal tissue.\(^1\) Thus, low-field ioMRI may be almost as effective as high-field ioMRS in differentiating normal tissue from residual tumor while being cheaper, logistically less intrusive, and relatively safer. This argument cannot be resolved with the available data. A study is needed to compare guided surgical resection with T2-weighted ioMRI versus ioMRS. Pamir and colleagues lay the groundwork for such a future randomized study that can cement the role of ioMRS in glioma surgery. Randomization of patients to one or the other resection strategy while cataloguing adverse events and final resection volume will solidify the argument that ioMRS allows safer maximal resection in comparison with traditional methods. In conclusion, this new study by Pamir et al.\(^5\) is creative and thought provoking and is likely to result in increasingly expanding applications of the multiple imaging modalities available with high-field ioMRI technologies.

\(\text{http://thejns.org/doi/abs/10.3171/2012.8.JNS121409}\)

**Disclosure**

The authors report no conflict of interest.

**References**


**Response**

**M. NECMETTIN PAMIR, M.D., AND KORAY ÖZDUMAN, M.D.**

Department of Neurosurgery, Actıbadem University School of Medicine, Istanbul, Turkey

We thank Drs. Shaikhouni and Chiocca for their insightful comments and for sharing their expertise in ioMRI technology. Low-grade glioma is not a benign disease but is one stage of a malignant disease process, with a 5-year survival rate of 59.9%.\(^1\) Surgery is the most effective form of treatment, but it is still far from perfect, as indicated by a 5-year tumor progression of more than 50% after neurosurgeon-determined gross-total resection.\(^6\) Therefore, novel technologies are needed to increase the extent of tumor resection and safety, with the eventual goal of an oncological resection.

The proven efficiency of ioMRI in increasing the extent of resection is solely based on intraoperative residual tumor detection.\(^2,4,5\) With the advent of advanced modalities, such as perfusion MRI, functional MRI, MRS, DWI, diffusion tensor imaging/tractography, high-definition fiber tracking, and quantitative diffusion tensor fiber tracking, MRI provides anatomical, metabolic, and clinical information on LGG that is beyond comparison with that obtained from early low-field scanners. Low-grade gliomas do extend beyond conventional MRI–defined borders where they can be detected using advanced sequences.\(^3,7\) Ultra high-field ioMRI carries this state-of-the-art MRI technology into the operating room. This is the very same technology that the surgeon uses to judge his own surgical results and monitor the clinical course, regrowth, and