Intraoperative ultrasound techniques for cerebral gliomas resection: usefulness and pitfalls

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Provenance and Peer Review: This article was commissioned by the editorial office, *Annals of Translational Medicine*. The article did not undergo external peer review.

Comment on: Liang C, Li M, Gong J, *et al.* A new application of ultrasound-magnetic resonance multimodal fusion virtual navigation in glioma surgery. Ann Transl Med 2019;7:736.

Submitted Feb 05, 2020. Accepted for publication Mar 12, 2020.

doi: 10.21037/atm.2020.03.178

View this article at: http://dx.doi.org/10.21037/atm.2020.03.178

Liang *et al.* described the application of navigated intraoperative ultrasound (N-ioUS), based on virtual fusion between real-time intraoperative ultrasound (ioUS) and preoperative magnetic resonance imaging (MRI), on a monocentric and retrospective series of supratentorial primary brain neoplasms operated on at the Third Affiliated Hospital of Sun Yat-sen University, China (1).

The technique consists on a navigated 2-dimensional B-mode ultrasound coupled with preoperative MRI and intraoperatively upgraded thanks to the system complementary options: fine-tuning to correct navigation-induced loss of accuracy, contrast-enhanced ultrasound (CEUS) to improve tumor borders detection, overlapping with preoperative morphological MRI and white matter fiber tracks reconstruction to better identify important structures (1). The authors used the fusion of all of these intraoperative data, resumed as US-MRI multimodal fusion virtual navigation system (UMNS), to assess some "warning points" (white matter fiber tracks were closed to MRI-defined tumor boundaries). These points were subsequently injected into the registered neuronavigation and used as guidance to obtain a maximal safe resection (1).

Forty-five patients from the same center were enrolled in a retrospective evaluation. Twenty-six patients were operated under UMNS guidance and 19 patients were operated with the assistance of ioUS alone, showing a higher rate of gross total resection in the UMNS group (84.6%) than in the ioUS group (31.6%), and showing a lower rate of postoperative morbidity at two weeks in the UMNS group (motor deficit 11.5%, aphasia 3.9%) than in the ioUS group (motor deficit 42.1%, aphasia 31.6%) (1). In addition, UMNS guidance showed a higher reliability in predicting the extent of resection (92.3%) than ioUS alone (42.1%) as observed on postoperative MRI (1). Image quality before dural opening was also improved by UMNS: in 13 cases after poor or moderate tumor visualization with ioUS alone, the UMNS guidance allowed improving tumor visualization from poor to moderate and from moderate to good images, using the image quality scale described by Solheim *et al.* (1,2). Interestingly, the whole process of injecting markers and scanning time using the UMNS guidance did not significantly increase the operating time compared to surgery with ioUS alone (1).

We commend the authors for their elegant study elucidating the utility of "advanced ultrasound techniques" and showing the possible value in daily neurosurgical practice. The main goal of surgical treatment both for high-grade and low-grade gliomas should be the achievement of the largest extent of resection while preserving the patient's neurological status and multiple studies have demonstrated that gross total resection is associated with improved survival rates (3,4). Various techniques have been developed to enhance the extent of resection of these challenging lesions while decreasing the rate of postoperative neurologic deficits, including MRI-based intraoperative neuronavigation, intraoperative MRI, fluorescein and 5-aminolevulinic acid guidance for high-grade gliomas, intraoperative functional brain mapping using direct electrical stimulations under awake condition, as well as ioUS. The present series represents a monocentric and retrospective effort, reporting better results both in terms of extent of resection and of postoperative outcome in a series of 45 supratentorial primary brain neoplasms encompassing well delineated WHO grades I gliomas and glioneuronal tumors and diffuse gliomas WHO grade II to IV.

ioUS represents a viable tool for neurosurgeons to refine the surgical management of gliomas: it is a low-cost, reliable, and fast technique that may reliably increase resection rates and decrease the residual tumor volume. Although most of the reported studies are monocentric and retrospective, as the present one, we observe an increasing interest from different groups. Here, UMNS usefully help neurosurgeons to obtain a better image quality than ioUS alone. These results could be possibly related to the varying neurosurgical experience (19 procedures with IoUS, 26 procedures with UMNS) and to the evolution of the respective use of ioUS and UMNS with time, which is not detailed in the results part. Inter-operator variability and the need of a specific training are the main pitfalls for application of ioUS in neurosurgery. This virtual navigation technique based on ioUS, aligned with preoperative MRI, was previously described for neurosurgical application by Prada *et al.* in 2014, highlighting the potential for brain shift correction and compensation of ioUS limitations, as the difficulties on orientation and lack of panoramic view (5). N-ioUS, associated to other ultrasound techniques as CEUS, may offer a feasible and low-resource technique, which could help less experienced neurosurgeons with ioUS images interpretation. In recent reports the use of 2-dimensional or 3-dimensional N-ioUS was associated with increased gross total resection rates and a low residual volume in high-grade and low-grade gliomas (6,7). As previously reported by some authors using similar N-ioUS techniques (8,9), UMNS showed good reliability and safety in detecting the tumor and a good accuracy of the navigation system, with a mean registration error of 1.5±0.6 mm, and the possibility to correct intraoperative error, due to brain shift, thanks to the fine-tuning based on ioUS images (1).

Beyond promising results of the present study, the reader should be aware of biases and limitations inherent to the retrospective design, to the non-homogeneous distribution of histopathological subtypes (high-grade and low-grade gliomas) and of tumor locations (eloquent and non-eloquent areas), which were not controlled. It is possible that additional factors may have contributed to the higher extent of resection we observe with the use of UMNS as compared to the use of ioUS alone.

Overall, it seems that UMNS may offer a low-cost, effective, and not time-consuming upgrade of ioUS, allowing an accurate intraoperative fusion with preoperative MRI, increasing tumor visualization, thanks to CEUS. According to the literature, B-mode images quality often diminishes during tumor removal due to the appearance of different artifacts reducing the sound-to-noise ratio between tumor remnants and reactive tissue changes (10). For this purpose, the use of CEUS could be effective on differentiating between tumor remnants and peritumoral edematous tissues by enhancing the hyper-vascularized tumor components (11,12). To reduce such artifacts, the Trondheim group is developing an acoustic coupling fluid that shows significantly less noise than ioUS images obtained with Ringer's solution (13). Finally, the system allows injecting elegantly some "warning points" into the navigated images to prevent such tagged eloquent structures to be damaged during tumor resection. Visualizing the limits between tumor borders and tagged eloquent structures reduced the occurrence of postoperative deficits although intraoperative imaging has previously shown its limitations in predicting functional areas and tracts location due to interindividual variability (14). A simpler way to identify and preserve eloquent white matter fiber pathways that has not been used in the present study, would be the use of intraoperative functional brain mapping using direct electrical stimulations under awake condition, especially for diffuse gliomas located in the dominant hemisphere (15).

UMNS, as well as all ioUS techniques, could be considered as potential tools in brain neoplasm surgery. It is mandatory for neurosurgeons who aim to adopt these techniques to pass through an initial learning curve in order to master advantages and limitations of this technique.

Acknowledgments

Funding: None.

Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.

org/10.21037/atm.2020.03.178). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Cite this article as: Moiraghi A, Pallud J. Intraoperative ultrasound techniques for cerebral gliomas resection: usefulness and pitfalls. Ann Transl Med 2020;8(8):523. doi: 10.21037/atm.2020.03.178