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Technical Note

Intraoperative augmented reality fiber tractography complements cortical and subcortical mapping

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ABSTRACT

Augmented reality (AR) has been found to be advantageous in enhancing visualization of complex neuroanatomy intraoperatively and in neurosurgical education. Another key tool that allows neurosurgeons to have enhanced visualization, namely of white matter tracts, is diffusion tensor imaging (DTI) that is processed with high-definition fiber tractography (HDFT). There remains an enduring challenge in the structural–functional correlation of white matter tracts that centers on the difficulty in clearly assigning function to any given fiber tract when evaluating them through separated as opposed to integrated modalities. Combining the technologies of AR with fiber tractography shows promise in helping to fill in this gap between structural–functional correlation of white matter tracts. This novel study demonstrates through a series of three cases of awake craniotomies for glioma resections a technique that allows the first and most direct evidence of fiber tract stimulation and assignment of function or deficit in vivo through the intraoperative, real-time fusion of electrical cortical stimulation, AR, and HDFT. This novel technique has qualitatively shown to be helpful in guiding intraoperative decision making on extent of resection of gliomas. Future studies could focus on larger, prospective cohorts of glioma patients who undergo this methodology and further correlate the post-operative imaging results to patient functional outcomes.

1. Introduction

Augmented reality (AR) has gained significant traction in the neurosurgical community as a novel adjunct not only for surgical and medical training but also for clinical use pre-operatively and intra-operatively. Although there remains a need for prospective randomized trials and there are still several technical challenges to be addressed with its deployment, AR has been found to be advantageous in enhancing visualization of complex neuroanatomy intraoperatively.[1–8] Another important tool that allows neurosurgeons to have an in vivo visualization of white matter tracts is diffusion tensor imaging (DTI)-based tractography, particularly when processed as high-definition fiber tractography (HDFT). HDFT is one of several advanced tractography processing approaches that permits visualization of crossing white matter trajectories at high resolutions.[9,10] HDFT has evolved into an important neurosurgical tool with key applications especially in glioma surgery that are propelled by its ability to enhance the surgeon's visualization of the white matter effects of tumor pathologies.[11] In presurgical planning applications, HDFT has shown promise in enabling accurate depictions of perilesional tracts in a 3-dimensional manner around gliomas to help plan for maximal extent of resections and even in identifying fiber tract infiltration in unprecedented detail to aid with surgical planning.[12–14] Nevertheless, there remains an enduring challenge in the structural–functional correlation of these white matter tracts that hinges on the difficulty in clearly assigning function to any given fiber tract when evaluating them through separated as opposed to integrated modalities. Combining the technologies of AR with fiber tractography shows promise in helping to fill in this gap between structural–functional correlation of white matter tracts.[15–17] Recent studies have explored whether fiber tract data can be reliably integrated through AR into standard neuro-navigation systems allowing for intraoperative visualization of major white matter tracts.[15,18,19] In this study,

Abbreviations: AR, Augmented reality; HDFT, high-definition fiber tractography; DTI, diffusion tensor imaging; ROI, regions of interest; SyncAR, 360 VR/AR surgical guidance platform; SMA, supplementary motor area; MRI, magnetic resonance imaging.

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we take these prior research efforts to the next level by demonstrating through a series of three cases of awake craniotomies for glioma resections a technique that allows the first and most direct evidence of fiber tract stimulation and assignment of function or deficit in vivo through the intraoperative, real-time fusion of electrical cortical stimulation, AR, and HDFT.

2. Methods

To generate the HDFT files for each patient model that would be used during surgical navigation, an AI algorithm was applied to a set of diagnostic magnetic resonance imaging (MRI) scans (DTI and a structural T1 pre-contrast). Alignment of the MRI scans is done automatically in the algorithm, and the bundles themselves are generated by a combination of seeding regions of interest (ROI) and manual refinement. Manual selection of the ROI and refining of the bundle is especially important for large tumors because the tracts are often significantly displaced, and the AI algorithm isn't as successful in locating the bundle.

Once the HDFT files have been generated, they are loaded into Surgical Theater's 360 V R/AR surgical guidance platform (SyncAR). The SyncAR is connected intraoperatively to the navigation system and surgical microscope to register the patient specific 360 V R model, including the HDFT files, to the stereoscopic imaging. Using augmented reality, the SyncAR shares the 3D images of the fiber tracts with the microscope and overlays this image on top of the field of view in the microscope. Alignment can be fine-tuned based on the parenchyma (sulci and gyri) and vascular landmarks (major cortical veins and arteries).

With the ability to choose which fiber bundles to see, and to turn this projection on and off, the surgeon can stereoscopically overlay these fiber tract images with their view of the cortex and white matter during awake surgery stimulation, providing a way to directly correlate functional information (electrical mapping results) with visualized fiber tracts via AR. In the following sections, this paper discusses the results of this surgical technique in conjunction with electrical cortical mapping across three different cases of awake craniotomies for tumor removal.

3. Results

The following three operative cases illustrate the utility of the novel approach of combining traditional intraoperative cortical and subcortical stimulation with augmented reality and HDFT to facilitate direct visualization of the fiber tracts that are being stimulated at both the cortical termination and at deeper levels within white matter.

Case 1. Left SMA low grade glioma: AR correlation of frontal aslant tract with speech arrest.

This patient was a 57-year-old who presented with sudden onset of seizures and imaging findings compatible with a low-grade glioma of the left supplementary motor area (SMA) (Fig. 1). Through a large frontal convexity craniotomy adjacent to the sagittal sinus, the cortex was exposed, and the origin of the tumor was identified at the left SMA's superior frontal gyrus anterior to a venous complex at the precentral sulcus. Direct electrical mapping of the cortex identified an area of speech arrest at the posterior-most aspect of our exposure in the SMA without a motor response. Starting at the posterior edge, the resection continued deeper into the white matter (Video 1). Subcortical stimulation in the deeper white matter yielded speech arrest again. Using AR overlay of the preoperative fiber tractography model onto the surgical field, we were able to directly visualize that the frontal aslant tract was being stimulated at the posterior limit of tumor resection. Then following an anatomical resection pathway using the superior frontal sulcus, a supra total resection of this tumor was achieved extending into the middle frontal gyrus with confirmation with mapping that there was no speech function in this area. The deep white matter portions of the resection were done under direct visualization of the stimulated aslant tract under AR tractography overlay. The deep margin of the tumor was the cingulate sulcus preserving both the cingulate tract and deep white matter in the centrum semiovale.

The postoperative course was characterized by improvement of the seizures and gross total resection at MRI. The pathology examination showed diffuse astrocytoma, IDH1 R132H mutant, WHO grade 2.

Case 2. Left temporal high-grade glioma: AR correlation of frontal AF branches with speech arrest

This is a 67-year-old male patient who presented with a first-time seizure episode, altered mental status, and expressive aphasia. Imaging findings were compatible with a high-grade glioma of the left temporal lobe centered in the fusiform gyrus (Fig. 2) who underwent a left awake frontotemporal craniotomy with cortical and subcortical electrical mapping in combination with AR for direct visualization of the white matter tracts. After the craniotomy, once the sylvian fissure and superior, middle, and inferior temporal gyri were identified, image guidance was employed with AR to identify the location of the fiber tracts and the tumor deep in the temporal lobe (Video 2). Electrical mapping in the cortex was deployed and a speech arrest region was identified in the ventral premotor cortex at the termination fibers of the arcuate fasciculus as visualized directly with AR integration of fiber tractography. No other areas of positive mapping were identified.

The postoperative course was uneventful with the improvement of preoperative symptoms and imaging showed complete tumor resection. Pathology reported gliosarcoma, IDH-WILDTYPE, WHO grade 4 and the patient underwent chemotherapy. After 1.5 years from the surgery, the patient underwent a second operation due to tumor regrowth. Postoperatively he had no complications and underwent radio and chemotherapy.

Case 3. Left supramarginal low-grade glioma: AR correlation of temporal AF branches with semantic paraphasias and temporo-parietal aslant tract with dissociation experience.

A 22-year-old male patient with a left supramarginal gyrus low-grade glioma presented with generalized seizures and mild speech impairment. The patient underwent a left parietal awake craniotomy with electrical cortical and subcortical mapping in combination with AR overlay of fiber tractography to facilitate recognition of the fiber tracts (Fig. 3). Positive cortical sites for facial numbness and twitching were identified at the postcentral gyrus. Semantic paraphasias were elicited at the superior temporal gyrus posteriorly and at anterior aspect of the angular gyrus but not at the supramarginal gyrus. These cortical positive sites corresponded to cortical branches of the arcuate fasciculus (Video 3). Interestingly, semantic paraphasias were elicited again by subcortical stimulation deep at the level of the temporo-parietal junction where the arcuate fasciculus is located and then just posteriorly at the level of the temporoparietal aslant tract, also known as vertical segment of the arcuate fasciculus; the patient also described an out-of-body experience or psychedelic dissociation experience when these areas were stimulated.[20],[21]

Postoperatively the patient presented transient speech and writing disturbance and short memory loss which recovered 3 months after surgery. Neuroimaging showed complete removal of the tumor. Pathology reported oligodendroglioma, IDH1 R132H-mutant and 1p/19q codeleted, WHO grade 2.

4. Discussion

Here we showcase a novel technique that allows for direct identification of fiber tract stimulation intraoperatively with the use of AR overlay of HDFT onto the operative field during awake craniotomy. Using this technique, we highlight the first evidence of fiber tract assignment of function or deficit in vivo through the intraoperative, real-time fusion of electrical cortical stimulation, AR, and HDFT. Prior to this combined stimulation and visualization methodology, the correlation of

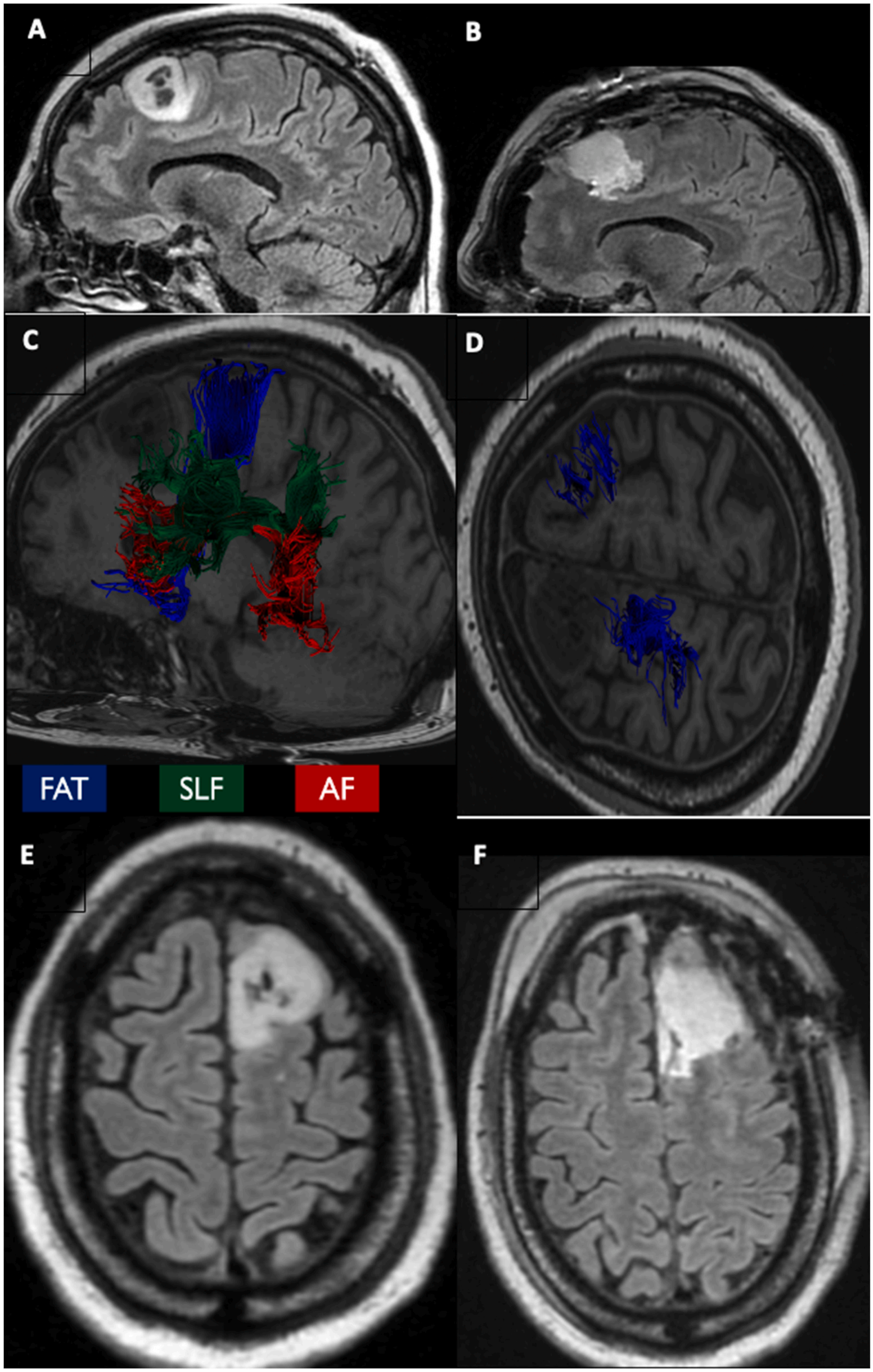

Fig. 1. A. Pre-operative sagittal FLAIR MRI showing a low-grade glioma of the left supplementary motor area
B.Post-operative sagittal FLAIR MRI
C. Sagittal T1 MRI showing the frontal aslant tract, superior longitudinal fasciculus, arcuate fasciculus
D.Axial T1 MRI showing the cortical projections of the frontal aslant tract
E.Pre-operative axial FLAIR MRI showing a low-grade glioma in the left supplementary motor area
F.Post-operative axial FLAIR MRI.

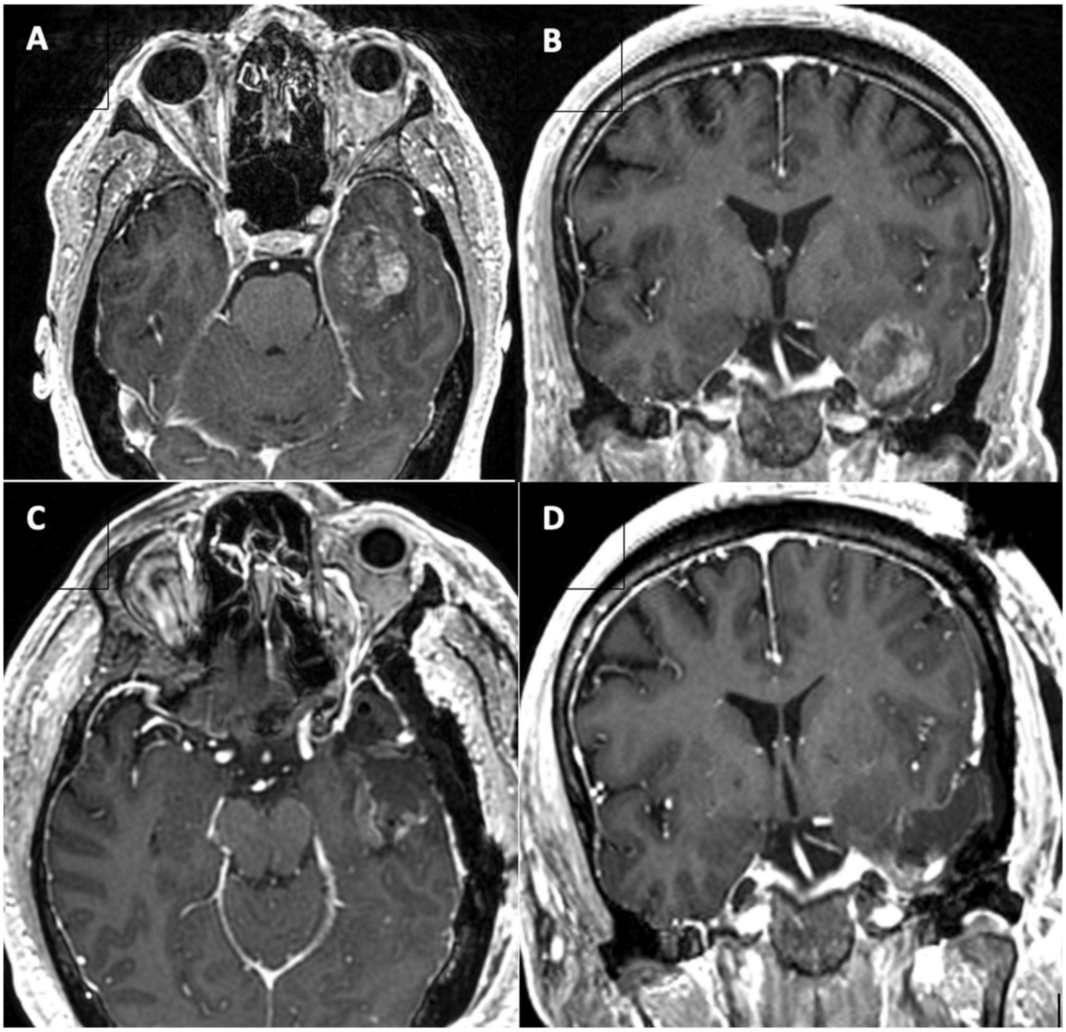

Fig. 2. A.Pre-operative axial T1 post-contrast MRI showing a high-grade glioma of the left temporal lobe centered in the fusiform gyrus.
B.Pre-operative coronal T1 post contrast MRI showing a high-grade glioma of the left temporal lobe
C.Post-operative axial T1 post contrast MRI
D. Post-operative coronal T1 post contrast MRI.

structure and function of fiber tracts has typically been done post-hoc based on postoperative tractography or intraoperatively based on image guidance that is detached from the direct AR navigation. It is important to note also that the deployment of this combined approach requires that the neurosurgeon and team have access to the intra-operative AR with a dedicated technical team.

There have been a few notable studies that have indirectly examined the structural and functional correlates of white matter tracts in the traumatic brain injury population by correlating analysis linking neuropsychological testing to HDFT.[22,23] The results from these studies show that the spatial properties of tractography may be altered in TBI, thus indirectly studying the structure and function relationship of fiber tracts. HDFT has also been used to better understand language pathways by correlating structural white matter changes with word production in stroke-related aphasia by applying an innovative approach known as connectometry.[24] Nevertheless, while these examples show the utility of correlating structural with behavioral measures, they do not directly address the enduring challenge of understanding the correlation of structure and function of white matter tracts and its clinical implications.

Other efforts to deal with the issue of correlating structure and function of white matter tracts and harnessing this information to direct clinical decision-making have involved referring to pre-operative tractography images intraoperatively and then comparing pre and post-operative functional testing for language deficits during glioma surgery.[25,26] While studies such as these allow for some correlation of structure and function, their approach is indirect and does not provide intraoperative information. Nevertheless, AR combined with HDFT and sodium fluorescein has been shown to assist in safe and effective maximal extent of resection and optimized patient outcomes.[17]

In this study, we have built upon these prior approaches of combining multimodal visualization methodologies such as AR and HDFT intraoperatively by directly adding cortical and subcortical stimulation to enhance our knowledge of structural–functional correlation of white matter tracts as a novel contribution to the field. This novel technique has shown to be helpful in guiding intraoperative decision making on extent of resection of gliomas. Future studies could focus on larger, prospective cohorts of glioma patients who undergo this methodology and further correlate the post-operative imaging results to patient functional outcomes and should also focus on the issue of brain shift during surgery and it's impact on AR overlays.

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The authors have no relevant disclosures to report.

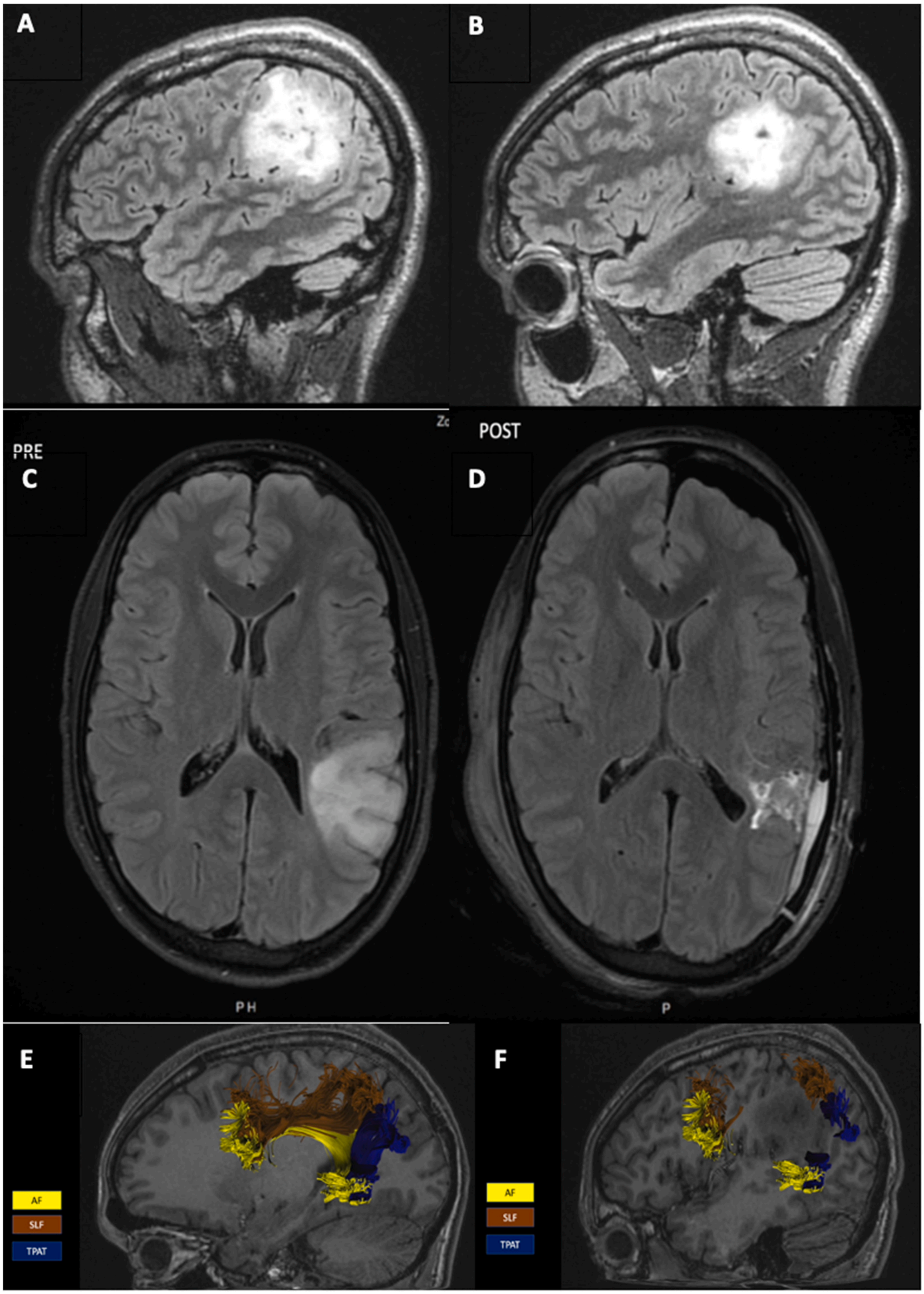

Fig. 3. A & B Pre-operative Axial FLAIR MRI showing a left supramarginal low-grade glioma
C.Pre-operative axial FLAIR MRI showing a left supramarginal low-grade glioma
D. Post-operative axial FLAIR MRI/
E. Deep projections of the temporoparietal aslant tract, arcuate fasciculus, superior longitudinal fasciculus
F. Cortical projections of the temporoparietal aslant tract, arcuate fasciculus, superior longitudinal fasciculus.

CRediT authorship contribution statement

Swathi Chidambaram: Conceptualization, Methodology, Resources, Validation, Writing – original draft, Writing – review & editing. **Diana Anthony:** Methodology, Resources, Writing – review & editing. **Tatiana Jansen:** Methodology, Resources, Writing – review & editing. **Vera Vigo:** Writing – review & editing. **Juan C. Fernandez Miranda:** Conceptualization, Methodology, Resources, Validation, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.wnsx.2023.100226.

References

1 Contreras López WO, Navarro PA, Crispin S. Intraoperative clinical application of augmented reality in neurosurgery: a systematic review. *Clin Neurol Neurosurg*. 2019; 177:6–11. https://doi.org/10.1016/j.clineuro.2018.11.018.

2 Meola A, Cutolo F, Carbone M, Cagnazzo F, Ferrari M, Ferrari V. Augmented reality in neurosurgery: a systematic review. *Neurosurg Rev*. 2017;40(4):537–548. https://doi.org/10.1007/s10143-016-0732-9.

3 Chidambaram S, Stifano V, Demetres M, et al. Applications of augmented reality in the neurosurgical operating room: a systematic review of the literature. *J Clin Neurosci Off J Neurosurg Soc Australas*. 2021;91:43–61. https://doi.org/10.1016/j.jocn.2021.06.032.

4 Mikhail M, Mithani K, Ibrahim GM. Presurgical and intraoperative augmented reality in neuro-oncologic surgery: clinical experiences and limitations. *World Neurosurg*. 2019;128:268–276. https://doi.org/10.1016/j.wneu.2019.04.256.

5 Louis RG, Steinberg GK, Duma C, et al. Early experience with virtual and synchronized augmented reality platform for preoperative planning and intraoperative navigation: a case series. *Oper Neurosurg Hagerstown Md*. 2021;21(4): 189–196. https://doi.org/10.1093/ons/opab188.

6 Haddad AF, Aghi MK, Butowski N. Novel intraoperative strategies for enhancing tumor control: future directions. *Neuro Oncol*. 2022;24(Supplement_6):S25–S32. https://doi.org/10.1093/neuonc/noac090.

7 Koike T, Kin T, Tanaka S, et al. Development of a new image-guided neuronavigation system: mixed-reality projection mapping is accurate and feasible. *Oper Neurosurg*. 2021;21(6):549–557. https://doi.org/10.1093/ons/opab353.

8 Turcotte EL, Jones BA, Chhabra N, et al. Awake microsurgical resection of a motor cortex glioma with cortical and subcortical motor mapping, image guidance, and augmented reality: 2-dimensional operative video. *Oper Neurosurg*. 2023;24(2). https://doi.org/10.1227/ons.0000000000000525. e122-e122.

9 Panesar SS, Abhinav K, Yeh FC, Jacquesson T, Collins M, Fernandez-Miranda J. Tractography for surgical neuro-oncology planning: towards a gold standard. *Neurother J Am Soc Exp Neurother*. 2019;16(1):36–51. https://doi.org/10.1007/s13311-018-00697-x.

10 Fernandez-Miranda JC, Pathak S, Engh J, et al. High-definition fiber tractography of the human brain: neuroanatomical validation and neurosurgical applications. *Neurosurgery*. 2012;71(2):430–453. https://doi.org/10.1227/NEU.0b013e3182592faa.

11 Henderson F, Abdullah KG, Verma R, Brem S. Tractography and the connectome in neurosurgical treatment of gliomas: the premise, the progress, and the potential. *Neurosurg Focus*. 2020;48(2):E6. https://doi.org/10.3171/2019.11.FOCUS19785.

12 Abhinav K, Yeh FC, Mansouri A, Zadeh G, Fernandez-Miranda JC. High-definition fiber tractography for the evaluation of perilesional white matter tracts in high-grade glioma surgery. *Neuro Oncol*. 2015;17(9):1199–1209. https://doi.org/10.1093/neuonc/nov113.

13 Celtikci E, Celtikci P, Fernandes-Cabral DT, Ucar M, Fernandez-Miranda JC, Borcek AO. High-definition fiber tractography in evaluation and surgical planning of thalamopeduncular pilocytic astrocytomas in pediatric population: case series and review of literature. *World Neurosurg*. 2017;98:463–469. https://doi.org/10.1016/j.wneu.2016.11.061.

14 Celtikci P, Fernandes-Cabral DT, Yeh FC, Panesar SS, Fernandez-Miranda JC. Generalized q-sampling imaging fiber tractography reveals displacement and infiltration of fiber tracts in low-grade gliomas. *Neuroradiology*. 2018;60(3):267–280. https://doi.org/10.1007/s00234-018-1985-5.

15 Nimsky C, Ganslandt O, Fahlbusch R. Implementation of fiber tract navigation. *Neurosurgery*. 2007;61(1 Suppl):306–317. https://doi.org/10.1227/01.neu.0000279224.83998.7d. discussion 317-318.

16 Luzzi S, Giotta Lucifero A, Baldoncini M, Del Maestro M, Galzio R. Postcentral gyrus high-grade glioma: maximal safe anatomic resection guided by augmented reality with fiber tractography and fluorescein. *World Neurosurg*. 2022;159:108. https://doi.org/10.1016/j.wneu.2021.12.072.

17 Luzzi S, Giotta Lucifero A, Martinelli A, et al. Supratentorial high-grade gliomas: maximal safe anatomical resection guided by augmented reality high-definition fiber tractography and fluorescein. *Neurosurg Focus*. 2021;51(2):E5. https://doi.org/10.3171/2021.5.FOCUS21185.

18 Ille S, Ohlerth AK, Colle D, et al. Augmented reality for the virtual dissection of white matter pathways. *Acta Neurochir*. 2021;163(4):895–903. https://doi.org/10.1007/s00701-020-04545-w.

19 Nimsky C, Bauer M, Carl B. Merits and limits of tractography techniques for the uninitiated. *Adv Tech Stand Neurosurg*. 2016;43:37–60. https://doi.org/10.1007/978-3-319-21359-0_2.

20 Panesar SS, Jta Belo, Yeh FC, Fernandez-Miranda JC. Structure, asymmetry, and connectivity of the human temporo-parietal aslant and vertical occipital fasciculi. *Brain Struct Funct*. 2019;224(2):907–923. https://doi.org/10.1007/s00429-018-1812-0.

21 Catani M, Mesulam M. The arcuate fasciculus and the disconnection theme in language and aphasia: history and current state. *Cortex J Devoted Study Nerv Syst Behav*. 2008;44(8):953–961. https://doi.org/10.1016/j.cortex.2008.04.002.

22 Presson N, Beers SR, Morrow L, et al. An exploratory analysis linking neuropsychological testing to quantification of tractography using High Definition Fiber Tracking (HDFT) in military TBI. *Brain Imaging Behav*. 2015;9(3):484–499. https://doi.org/10.1007/s11682-015-9386-4.

23 Ware AL, Biekman B, Hachey R, et al. A preliminary high-definition fiber tracking study of the executive control network in blast-induced traumatic brain injury. *J Neurotrauma*. 2019;36(5):686–701. https://doi.org/10.1089/neu.2018.5725.

24 Hula WD, Panesar S, Gravier ML, et al. Structural white matter connectometry of word production in aphasia: an observational study. *Brain J Neurol*. 2020;143(8): 2532–2544. https://doi.org/10.1093/brain/awaa193.

25 Kuhnt D, Bauer MHA, Becker A, et al. Intraoperative visualization of fiber tracking based reconstruction of language pathways in glioma surgery. *Neurosurgery*. 2012;70 (4):911–919. https://doi.org/10.1227/NEU.0b013e318237a807. discussion 919-920.

26 Nimsky C, Ganslandt O, Hastreiter P, et al. Preoperative and intraoperative diffusion tensor imaging-based fiber tracking in glioma surgery. *Neurosurgery*. 2007;61(1 Suppl):178–185. https://doi.org/10.1227/01.neu.0000279214.00139.3b. discussion 186.