Using Quicktome for Intracerebral Surgery: Early Retrospective Study and Proof of Concept

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■ BACKGROUND: **Neurosurgeons have limited tools in their armamentarium to visualize critical brain networks during surgical planning. Quicktome was designed using machine-learning to generate robust visualization of important brain networks that can be used with standard neuronavigation to minimize those deficits. We sought to see whether Quicktome could help localize important cerebral networks and tracts during intracerebral surgery.**

■ METHODS: **We report on all patients who underwent keyhole intracranial surgery with available Quicktome-enabled neuronavigation. We retrospectively analyzed the locations of the lesions and determined functional networks at risks, including chief executive network, default mode network, salience, corticospinal/sensorimotor, language, neglect, and visual networks. We report on the postoperative neurologic outcomes of the patients and retrospectively determined whether the outcomes could be explained by Quicktome's functional localizations.**

■ RESULTS: **Fifteen high-risk patients underwent craniotomies for intra-axial tumors, with the exception of one meningioma and one case of leukoencephalopathy. Eight patients were male. The median age was 49.6 years. Quicktome was readily integrated in our existing navigation system in every case. New postoperative neurologic deficits occurred in 8 patients. All new deficits, except for one resulting from a postoperative stroke, were expected and could be explained by preoperative findings by Quicktome. In addition, in those who did not have new neurologic deficits, Quicktome offered explanations for their outcomes.**

■ CONCLUSIONS: **Quicktome helps to visualize complex functional connectomic networks and tracts by seamlessly integrating into existing neuronavigation platforms. The added information may assist in reducing neurological deficits and offer explanations for postsurgical outcomes.**

INTRODUCTION

Surgery for intra-axial lesions carries risks of incurring neurologic deficits. Complications may be mitigated by increasing pre- and intraoperative information and integrating that information with navigational tools combined with functional magnetic resonance imaging (fMRI) and diffusion tractography imaging (DTI).[1-3] However, fMRI is task-based and relies on patient participation, and DTI provides only limited information on basic functional networks and bound by the fact that they are anatomically based.[4] They do not yield information on important brain networks that may result in other neuropsychological sequelae if transgressed.[5]

Quicktome (Omniscient Neurotechnology; Perth, Australia) is a software developed based on the Human Connectome Project (HCP) as a surgical tool to help neurosurgeons visualize important functional networks on frameless stereotaxis.[5,6] It exceeds the limitations of conventional DTI and fMRI, as it uses resting-state data and determines anatomical localizations of important cerebral networks, such as central executive network (CEN),

Key words
- Connectomics
- Functional MRI
- Intra-axial surgery
- Quicktome
- Tumor

Abbreviations and Acronyms
CEN: Central executive network
DMN: Default mode network
DTI: Diffusion tractography imaging
fMRI: Functional magnetic resonance imaging
GTR: Gross total resection
HCP: Human Connectome Project

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default mode network (DMN), salience network, language network, limbic pathways, sensorimotor network, and visual pathways (subdivisions of these networks are also possible).[7,8] Its principal advantage from the time of conception is the fact that the illustrated networks are based on tractography at the individual level and can be integrated into existing frameless stereotactic systems.

In the present study, we report on our initial experience using Quicktome for mainly intra-axial tumor surgery with the exception of one meningioma and one case of leukoencephalopathy. Our primary aim was to see whether the Quicktome software can be integrated into standard neuronavigation and the standard neurosurgical workful. For the second aim, although we performed the aforementioned surgeries using our standard keyhole principles, we hypothesized and investigated in a retrospective manner, akin to a thought experiment, that Quicktome could help localize important cerebral networks relevant to each lesion to inform preoperative risk assessments and potential avoidance of transgressing those networks and incurring unwanted neurological deficits. We report on its feasibility, ease of use, and lessons learned by retrospectively reviewing surgeries performed using Quicktome as a surgical adjunct.

METHODS

Patient Selection

All patients with intra-axial tumors who had undergone surgical resection at the Centre for Minimally Invasive Neurosurgery (Sydney, Australia) using Quicktome as an adjunct to standard frameless stereotaxis (Brainlab, Munich, Germany) were reviewed. This study was approved by the Human Research Ethics Committee of the South Eastern Sydney Local Health District (2021/ETH00195). Patient consent was waived ethics committee due to the retrospective nature. Of note, surgical decisions were not made using Quicktome and were recommended based on our usual practice. We collected information on demographics, perceived neurologic functions at risk from each surgery, and whether the function was affected postsurgery. Every patient was followed for at least 30 days after surgery to assess perioperative outcomes. We retrospectively reviewed whether Quicktome was able to explain anticipated neurological deficits after surgery.

Quicktome Processing

Every patient underwent MRI of the brain with intravenous gadolinium, including T1-weighted sequence suitable for neuronavigation and a resting-state MRI. The DICOM (Digital Imaging and Communications in Medicine) images are then processed in the Omniscient cloud-based software (approximately 30 minutes), which employs machine learning-based technique for parcellating a brain as previously described.[5] The processed images can then be directly uploaded onto a navigation either through PACS (picture archiving and communication system) or manually using a data drive. It differs from other DTI protocol by using several proprietary algorithms to enable the construction of a personalized brain map based on connectivity. Raw MRI scans underwent a series of steps that correct for noise, including gradient distortion correction and subject motion correction. Quicktome automatically employs edema correction to better visualize peritumoral tracts. The workflow and user interface are demonstrated in supplemental digital content.

Constrained spherical deconvolution is used to model multiple tracts crossing the same region.[9] Structural connectivity atlasing is applied to determine parcellation locations based on their connections, regardless of how they have been altered by the tumor (unpublished method).[10] The authors trained a machine-learning model using the HCP Multi-Modal Parcellation, version 1.0, atlas based on diffusion tractography structural connectivity to learn the connectivity patterns between each parcellations and those to which they connect (unpublished method).[6] Q2

This model is used to classify held out parcellations by warping the HCP atlas to the patient's brain and collecting a set of feature vectors of the connectivity of each voxel. The feature vectors are then used to determine each voxel parcellation identity. This creates a voxel-per-voxel version of the HCP atlas with subcortical components that is not dependent on brain shape or pathologic distortion and is patient-specific but also comparable between patients. Specific functional networks with their tracts joining specific parcellations are then super-imposed onto a T1-weighted reference image for surgical navigation.

Intraoperative Workflow

Neuronavigation (Brainlab) was set up after the patient's head was fixed with the Mayfield head holder. A keyhole, minimally invasive approach was planned to sufficiently encompass a craniotomy that was tailored to the long axis of the tumor and depth and diameter of the tumor.[11] Quicktome was integrated into standard neuronavigation in every case to test the successful marriage of the two platforms.

Surgical Outcome Assessment

Radiographic assessments were determined by authors C.T. and J.Y. Gross total resection (GTR) was defined as removal of all T1-weighted contrast enhancement (glioblastoma, meningioma, radiation necrosis) or noncontrast-enhancing component (e.g., low-grade oligodendroglioma) depending on the pathologies. Near-total resection was defined as incomplete but greater than 95% of the aforementioned components. Subtotal resection was defined as under 95% of the lesion. Both expected and unexpected postoperative deficits were retrospectively queried and assessed by authors (C.T., J.Y., M.S.) as to whether they could be explained by adjacent parcellations and tracts demonstrated by Quicktome.

RESULTS

A total of 15 patients underwent craniotomies for tumor resection using Quicktome-enabled neuro-navigation (Table 1). Eight patients were male. The median age was 49.6 years (interquartile range 40.0–68.3). Quicktome was properly integrated in our existing navigation system in every case. New postoperative neurologic deficits occurred in 8 patients. In these patients, all the new deficits could be explained by Quicktome as the areas surgically transgressed involved the networks and tracts at risk, including patient 2, who suffered a posterior temporal stroke. In addition, those who did not have new neurologic deficits were

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Table 1. Patient Demographics and Clinical Information

Patient	Sex	Age, years	Location	Pathology	Preoperative Symptoms	Networks/Tracts at Risk	Ability to Localize Lesion	Procedure	Extent of Resection	Neurologic Outcome (Expected?)	Outcomes Explained by Quicktome?
1	m	67.9	Right temporal	Radiation Necrosis	N/A	CST	yes	Lesionectomy	GTR	Transient hemiparesis (yes)	Yes
2	f	40.0	Left temporo-insular	Anaplastic Astrocytoma	Speech arrest/ seizure	CST Language Salience	yes	Lesionectomy	GTR	Posterior temporal stroke (no) Expressive Dysphasia (no) Retained receptive language function (yes) Exacerbation of major depressive disorder (no)	Yes
3	m	44.1	Right frontal pre-motor	Anaplastic oligodendroglioma	Seizure	sensorimotor/CST	yes	Lesionectomy	GTR	Transient hemipresis (yes)	Yes
4	m	76.5	Left temporal	Recurrent GBM	Confusion global aphasia	CST DMN Language Optic radiations	yes	Temporal lobectomy	GTR	Confusion, Global Aphasia (yes)	Yes
5	f	38.6	Right fronto-temporal	Recurrent GBM	N/A	CEN DMN CST	yes	Lesionectomy	GTR	No new deficits	Yes
6	m	36.6	Right frontal motor	Recurrent Grade 2 astrocytoma	N/A	CST	yes	Lesionectomy	GTR	Transient hemiparesis (yes)	Yes
7	m	49.4	Left inferior frontal gyrus and pre-motor	Anaplastic Astrocytoma	Right sided hemiparesis Expressive dyspasia	CST/sensorimotor Language	yes	Lesionectomy	NTR	Transient hemiparesis (yes)	Yes
8	f	25.4	Left frontopolar	Recurrent GBM	Seizure	CEN CST language salience	yes	Frontal supramaximal lobectomy	GTR	No new deficits	Yes
9	f	61.2	Left occipital	GBM	Seizure Right homonymous hemianopsia	CST DMN neglect Visual	yes	Occipital supramaximal lobectomy	GTR	No new deficits	Yes
10	m	49.6	Right posterior temporal	Recurrent GBM	N/A	CEN CST DMN neglect Visual	yes	Lesionectomy	NTR	No new deficits	Yes

m, male; N/A, not available; CST, xxx; GTR, gross total resection; f, female; DMN, default mode network; CEN, central executive network; NTR, near-total resection; GBM; glioblastoma; STR, subtotal resection.

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Table 1. Continued

Patient	Sex	Age, years	Location	Pathology	Preoperative Symptoms	Networks/Tracts at Risk	Ability to Localize Lesion	Procedure	Extent of Resection	Neurologic Outcome (Expected?)	Outcomes Explained by Quicktome?
11	f	44.9	Left frontal parafalcine	Atypical meningioma	N/A	CST CEN DMN language salience	yes	Lesionectomy	GTR	No new deficits	Yes
12	m	68.3	Left frontal pre-motor	Grade 2 oligodendroglioma	N/A	CEN DMN Language sensorimotor/CST Salience	yes	Lesionectomy	GTR	No new deficits	Yes
13	m	51.5	Right motor subcortical	Leukoencephalopathy	Left sided hemiparesis	CEN CST/sensorimotor DMN	yes	Open biopsy/ lesionectomy	STR	Increased left sided hemiparesis (yes)	Yes
14	f	72.0	Left parieto-occipital	GBM	Confusion Imbalance right-sided hemi-sensory neglect	CST DMN Language Optic radiations	yes	Lesionectomy	GTR	Right homonymous hemianopsia (yes) right sided hemi-sensory neglect (yes)	Yes
15	f	79.3	Left posterior temporal	GBM	Speech arrest/ seizure	CST IFOF language optic radiations	yes	Lesionectomy	GTR	No receptive language deficits (yes)	Yes

m, male; N/A, not available; CST, xxx; GTR, gross total resection; f, female; DMN, default mode network; CEN, central executive network; NTR, near-total resection; GBM; glioblastoma; STR, subtotal resection.

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investigated and Quicktome offered explanations such as either the preoperative deficits were from tumor involvement or the lesion did not encompass or involve the parcellations and tracts at risk.

Illustrative Cases

Patient 2. Patient 2 was a 40-year-old, right-handed White female with a history of major depressive disorder who presented a seizure that involved sensory disturbance and speech arrest. MRI revealed a large, left-sided insular glioma with faint gadolinium enhancement and extension into her superior temporal gyrus (Figure 1A).

An extensive discussion was conducted with the patient explaining the benefits and risks of awake craniotomy compared to asleep craniotomy. The patient elected to undergo the procedure asleep with the goal of surgery being radiographic maximal resection of the tumor. A mini-pterional craniotomy was performed to allow a transcortical approach to the superficial portion of the tumor with the shortest transcortical distance and with a slight anterior-to-posterior bias and to allow unimpeded access to the insular component. Upon detailed retrospective review, Quicktome revealed the receptive speech (Wernicke) area to be immediately posterior to her tumor that extended to the superior temporal gyrus (Figure 1B). Quicktome noted that tumor-involving temporal portion as being noneloquent, and it was resected along with the insular tumor itself. The salience network on the left also was compressed by the tumor near the anterior insula.

Postoperatively, the patient's ability to understand language was retained, but she was noted to have occasional word-finding difficulties. Postoperative MRI demonstrated GTR of the tumor (anaplastic astrocytoma) and an unexpected posterior temporal stroke (Figure 1C and D). At postoperative follow-up, she continued to have improvements with her speech, specifically with only seldom word-finding errors. However, she had exacerbated symptoms from her preoperative major depression and violent mood swings towards her family members that required further treatment.

Patient 6. Patient 6 was a 37-year-old male who was diagnosed and operated on in 2013 for a right frontal pre-motor low-grade glioma. He presented with a T1 hypointense nodule in the posterior portion of his surgical cavity that had increased in size during serial MRIs (Figure 2A). Due to the tumor's location, extensive counseling was conducted regarding possible weakness after surgery as the tumor progression was occurring in the motor area. The patient elected to proceed with surgery having understood that risk.

We performed a redo right frontal keyhole (asleep) craniotomy with trans-sulcal approach to the lesion. GTR of the lesion was achieved (Figure 2C). The patient exhibited transient weakness in his left arm and leg that had recovered by postoperative day 1. Quicktome image was reviewed to analyze the sensorimotor cortical representation and the corticospinal tract.[12] It was noticed the offending lesion did not involve the corticospinal tract (Figure 2B).

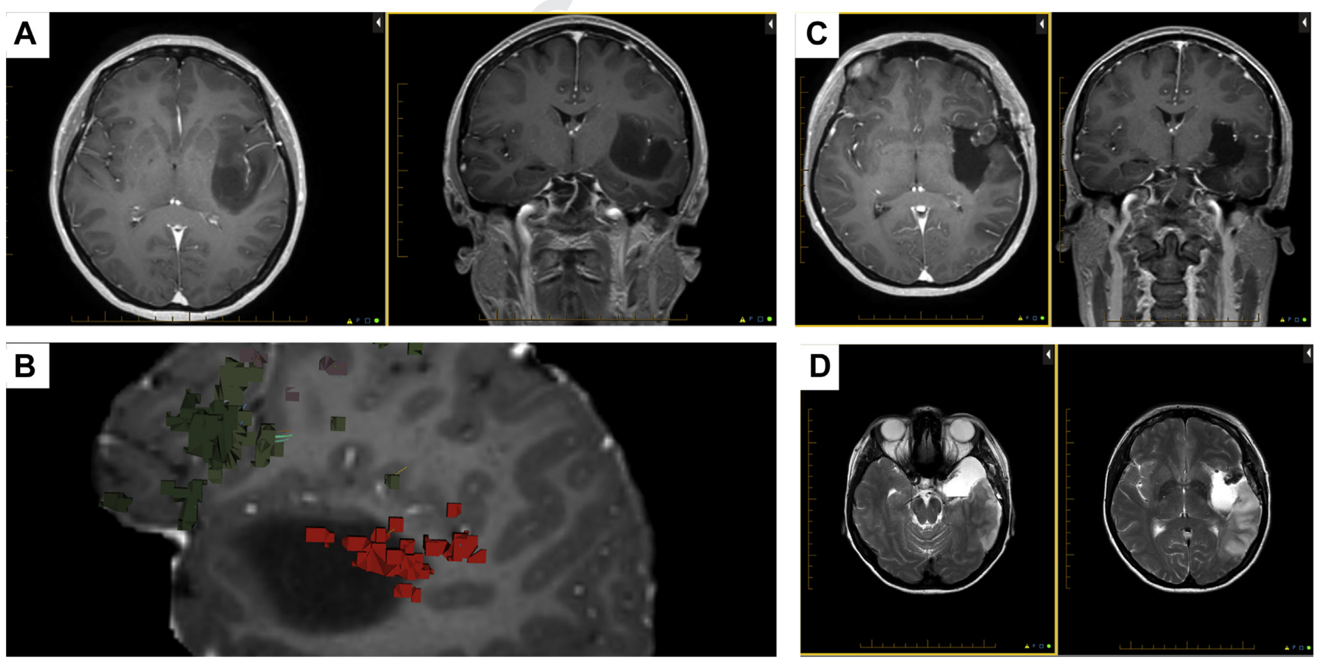

Figure 1. Resection of left insular glioma. (**A**) Axial (*left*) and coronal (*right*) T1-weighted gadolinium-enhanced magnetic resonance imaging (MRI) demonstrates an insular tumor with extension into the superior temporal gyrus. (**B**) Quicktome software demonstrates an expressive area (*dark green*) and receptive area (*red*) that are connected by arcuate fasciculus (not shown). (**C**) Axial (*left*) and coronal (*right*) T1-weighted gadolinium-enhanced MRI demonstrates gross total resection of the tumor. (**D**) Axial T2-weighted MRI (inferior temporal cut on left, more superior cut on right) demonstrates a stroke involving the posterior temporal lobe.

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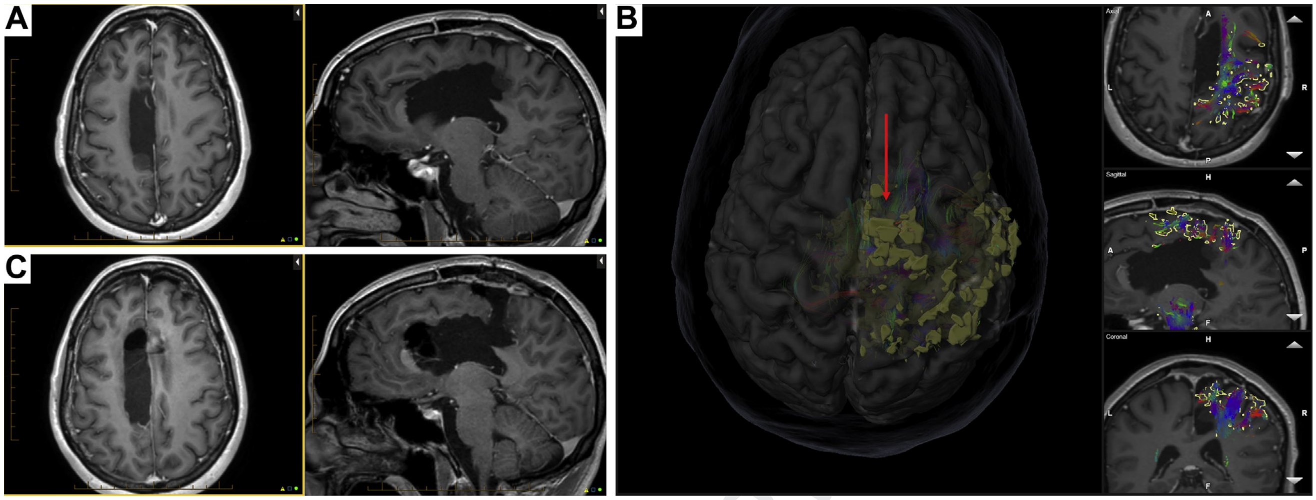

Figure 2. Resection of right motor glioma. (**A**) Axial (*left*) and sagittal (*right*) T1-weighted gadolinium-enhanced magnetic resonance imaging (MRI) demonstrates a nonenhancing tumor in the posterior portion of the prior surgical cavity. (**B**) Quicktome software (craniotomy planning view on *top left*) demonstrates that the tumor did not involve any corticospinal tract in axial (*top right*), sagittal (*bottom left*), and coronal views (*bottom right*). The *red arrow* indicates the approximate entry point of our trans-sulcal approach to the tumor. (**C**) Axial (*left*) and sagittal (*right*) T1-weighted gadolinium-enhanced MRI demonstrates gross total resection of the tumor.

Patient 15. Patient 15 was a 79-year-old, right-handed, Chinese female with a history of atrial fibrillation who presented with speech arrest. An MRI was performed that demonstrated a contrast-enhancing tumor in the left posterior temporal lobe (Figure 3A). She was neurologically intact at presentation. Importantly, she spoke mostly Shanghainese, a Chinese dialect, and only seldomly Mandarin Chinese.

The patient and her family elected to proceed for maximal resection due to her elderly age and predilection for a rare Chinese dialect. As the tumor was near the cortical surface, neuronavigation was used in the typical fashion to tailor a keyhole craniotomy for the tumor (Figure 3C). GTR was achieved (Figure 3D). When analyzing parcellations and tracts involved in language using Quicktome, an area in the inferior frontal gyrus was noted, presumably Broca's area, that was connected to 2 areas via the arcuate and superior longitudinal fasciculus (Figure 3B). The arcuate fasciculus branched into 2 areas, one in the posterior superior temporal gyrus (stereotypical Wernicke area) and another in the parietal lobe, which appeared to be very robust and was connected to the supplementary motor area via the superior longitudinal fasciculus. The tumor was noted to encompass the entirety of the posterior temporal language parcellations.

Postoperatively, the patient had no visual field cut and did not have any receptive language deficit. Most interestingly, she spoke more Mandarin than Shanghainese, when compared with before surgery, and this was corroborated by her family members.

DISCUSSION

We report our initial experience using Quicktome as a possible surgical adjunct to standard neuronavigation in understanding complex functional connectomic networks and tracts in the context of intracranial surgery. We demonstrate Quicktome's integration to the routine neurosurgical workflow and its potential to provide insight into not only neurosurgical planning but also functional explanations for neurological outcomes after intra-axial tumor surgery. We discuss to follow important lessons and limitations derived from our initial experience using this software as a surgical planning tool.

Ability to Visualize Important Networks and Pathways

Our initial experience with the software shed light into its potential in obviating the need for traditional awake craniotomy for language mapping.[13] For instance, in patient 2, who decided to have asleep craniotomy for radical resection of her insular tumor (a decision made independent of the implementation of this software), we were able to clearly visualize the receptive area of her language pathways, and perform her surgery in an asleep manner. Patients with insular gliomas benefit from maximal tumor resection.[14-16] Multiple reports in the literature illustrate the benefits of awake craniotomy in localizing important language areas and corticospinal tracts.[13,17-19] We were able to perform a radical temporal lobectomy, which allowed for easy access and visualization of the insular cortex. A review of the preoperative Quicktome images localized the cortical representation of her receptive language area. As her tumor was clearly delineated from normal tissue due to its consistency, GTR was achieved with the medial border as well. In patient 6, the fact that the low-grade astrocytoma did not demonstrate any involvement of the corticospinal tract suggested that there may have been remodeling of the tract over time and likely allowed for safe resection of the tumor.[20] Similarly, patient 8, a 25-year-old young female with a left frontal recurrent glioblastoma, had baseline anxiety that made her a poor

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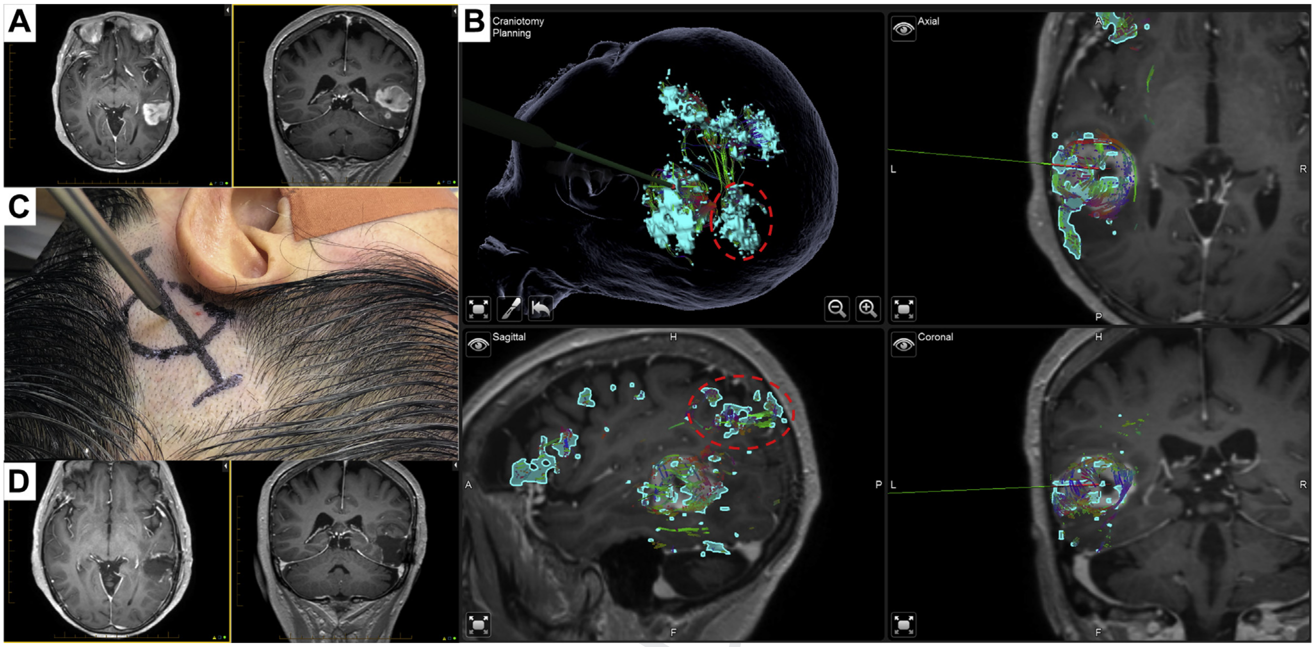

Figure 3. Resection of left posterior temporal glioblastoma. (**A**) Axial (*left*) and coronal (*right*) T1-weighted gadolinium-enhanced magnetic resonance imaging (MRI) demonstrates a gadolinium-enhancing mass in the left posterior temporal lobe. (**B**) Quicktome software applied to standard neuronavigation demonstrates language parcellations (*aqua*) encapsulated within the tumor mass (craniotomy planning view on *top left,* axial — *top right,* sagittal — *bottom left,* coronal — *bottom right*). *Dotted circles* indicated robust parietal component of language network. (**C**) Tailored keyhole craniotomy based on neuronavigation. The patient and her family provided consent for the publication of the image. (**D**) Axial (*left*) and coronal (*right*) T1-weighted gadolinium-enhanced MRI demonstrates gross total resection.

candidate for awake surgery if we elected to perform a supramaximal resection. Quicktome theoretically would be able to provide the outline of the posterior cut as part of the presurgical planning compared with going by anatomical landmarks instead. In patient 15, the tumor clearly encapsulated the posterior temporal component of the language network and was near the surface. With that knowledge, there was little utility in performing that surgery in an awake manner. fMRI could be performed in an otherwise English-speaking patient but this was not feasible with this patient who speaks a very select Chinese dialect. We could argue in our thought experiment that with Quicktome, the decision to undergo asleep craniotomy was logically made and we could avoid subjecting the elderly patient to undue stress from an awake craniotomy. Of note, despite the preoperative concern for receptive language deficit, the patient was able to retain language comprehension. This type of scenario after resection of the Wernicke area has been documented before and may involve recruiting areas immediately around the lesion or the involvement of remote networks; in this case the patient's robust parietal hub as part of the language network and her bilingual, Chinese background may indicate the involvement of the right hemisphere as well.[21-23]

Preoperative Discussion of Surgical Risks

Comprehensive presurgical discussions necessitate detailed explanations of the benefits and risks of the surgery. Especially in neuro-oncologic surgery, the goal of maximal tumor resection must be balanced with potential neurologic deficits that may result. Using Quicktome to visualize important network and tracts, we can better inform patients and their families on expected outcomes, especially if aggressive surgical resections are to be offered. For example, patient 13 had a ring-enhancing lesion with a known diagnosis of adult-onset leukoencephalopathy. A biopsy was requested by his multidisciplinary team to confirm the diagnosis, given his progressive hemiparesis. Quicktome demonstrated the CST traversing partially through the highly edematous lesion, which may limit traditional DTI, and, therefore, we could in theory better inform the patient and the family that post-operative deficit, namely increased hemiparesis, would be expected.[24,25]

Explanations of Noncanonical Postoperative Deficits

Cognitive dysfunction after glioma surgery is a well-documented phenomenon and is increasingly being recognized.[26-30] However, the neuro-oncologic surgical community currently does not have an intuitive tool to account for these atypical postoperative deficits that are outside the realm of basic (i.e., motor and visual) functions. In patient 2, her postoperative exacerbation of major depressive symptoms, which is a known phenomenon after glioma surgery, and violent mood swings toward others was readily explained by the Quicktome software, which demonstrated her salience network to be involved, displaced, and somewhat encompassed by the insular component of the tumor.[31] Anatomically, the anterior insular cortex serves as a main hub of the salience network, involving motivation and behavior to respond compassionately to another person's feelings and the evaluation of internal and external sensory information.[32-34] The salience network has been implicated in major depressive disorder (emotional pain) and it has known functions in empathy and mood stability.[35-37] The Quicktome software allowed us to readily visualize whether any other noncanonical pathways, such as CEN and DMN, were involved in the surgical access to each applicable lesion. Further neuropsychological outcomes following glioma surgery will be the focus of a proposed Glioma Connectome Project using the Omniscient software.

Limitations

The current study is based on our initial experience of using a proprietary software in development. Although it was not a systemically designed study, it provided insights into the potential of such a software package in surgical planning from preoperative discussions to intraoperative decision-making. The authors recognized that the application of Quicktome will have to be explored in a systematic fashion to ensure external generalizability. Its ability to aid in language and motor cortical surface mapping, in addition to other neurocognitive functioning, will have to be assessed together with conventional intraoperative stimulation. At this time, we as a field do not definitely understand the essentiality or redundancy for each hub in a given network. Like most neuronavigation adjuncts, it does not account for brain shift during tumor resection. Currently, Quicktome is limited to processing language pathways with the assumption of left hemispheric dominance and the use of western languages. Development is in progress in providing a solution for more individualized language network localization via machine learning over large databases of healthy individuals. Its ability to visualize more complex functional connectomic networks, such as CEN, DMN, and salience is first of its kind and the potential sequelae from their transgressions will have to be assessed with neuropsychological batteries, which will be the subject of a proposed Glioma Connectome Project.

CONCLUSIONS

Quicktome could be readily integrated into existing neuronavigation platforms to help visualize complex functional connectomic networks and tracts. It has the potential to enhance surgical planning and predictions for neurological outcomes after intracerebral surgeries.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Jacky T. Yeung: Conceptualization, Methodology, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Hugh M. Taylor:** Data curation, Software. **Peter J. Nicholas:** Data curation, Software. **Isabella M. Young:** Writing – review & editing. **Ivy Jiang:** Visualization. **Stephane Doyen:** Software, Writing – review & editing. **Michael E. Sughrue:** Conceptualization, Methodology, Software, Formal analysis, Writing – review & editing, Supervision. **Charles Teo:** Conceptualization, Methodology, Formal analysis, Writing – review & editing, Supervision.

REFERENCES

1. Orringer DA, Golby A, Jolesz F. Neuronavigation in the surgical management of brain tumors: current and future trends. *Expert Rev Med Devices*. 2012;9:491-500.
2. Sommer B, Grummich P, Coras R, et al. Integration of functional neuronavigation and intraoperative MRI in surgery for drug-resistant extratemporal epilepsy close to eloquent brain areas. *Neurosurg Focus*. 2013;34:E4.
3. Hall WA, Kim P, Truwit CL. Functional magnetic resonance imaging-guided brain tumor resection. *Top Magn Reson Imaging*. 2009;19:205-212.
4. Azad TD, Duffau H. Limitations of functional neuroimaging for patient selection and surgical planning in glioma surgery. *Neurosurg Focus*. 2020;48:E12.
5. Yeung JT, Taylor HM, Young IM, Nicholas PJ, Doyen S, Sughrue ME. Unexpected hubness: a proof-of-concept study of the human connectome using pagerank centrality and implications for intracerebral neurosurgery. *J Neurooncol*. 2021;151:249-256.
6. Glasser MF, Coalson TS, Robinson EC, et al. A multi-modal parcellation of human cerebral cortex. *Nature*. 2016;536:171-178.
7. Jones RG, Briggs RG, Conner AK, et al. Measuring graphical strength within the connectome: a neuroanatomic, parcellation-based study. *J Neurol Sci*. 2020;408:116529.
8. Briggs RG, Conner AK, Baker CM, et al. A Connectomic atlas of the human cerebrum-chapter 18: the connectional anatomy of human brain networks. *Oper Neurosurg (Hagerstown)*. 2018;15(suppl_1):S470-S480.
9. Farquharson S, Tournier JD, Calamante F, et al. White matter fiber tractography: why we need to move beyond DTI. *J Neurosurg*. 2013;118:1367-1377.
10. Tournier JD, Yeh CH, Calamante F, Cho KH, Connelly A, Lin CP. Resolving crossing fibres using constrained spherical deconvolution: validation using diffusion-weighted imaging phantom data. *Neuroimage*. 2008;42:617-625.
11. Teo C. The concept of minimally invasive neurosurgery. *Neurosurg Clin N Am*. 2010;21:583-584. v.
12. Baker CM, Burks JD, Briggs RG, et al. A connectomic atlas of the human cerebrum-chapter 3: the motor, premotor, and sensory cortices. *Oper Neurosurg (Hagerstown)*. 2018;15(suppl_1):S75-S121.
13. Haglund MM, Berger MS, Shamseldin M, Lettich E, Ojemann GA. Cortical localization of temporal lobe language sites in patients with gliomas. *Neurosurgery*. 1994;34:567-576 [discussion: 576].
14. Sughrue M, Bonney PA, Burks JD, et al. Multilobar insular-involving gliomas: results with hyperaggressive resection. *Cureus*. 2017;9:e1623.
15. Wang DD, Deng H, Hervey-Jumper SL, Molinaro AA, Chang EF, Berger MS. Seizure outcome after surgical resection of insular glioma. *Neurosurgery*. 2018;83:709-718.
16. Aghi MK, Nahed BV, Sloan AE, Ryken TC, Kalkanis SN, Olson JJ. The role of surgery in the management of patients with diffuse low grade glioma: a systematic review and evidence-based clinical practice guideline. *J Neurooncol*. 2015;125:503-530.
17. Sanai N, Mirzadeh Z, Berger MS. Functional outcome after language mapping for glioma resection. *N Engl J Med*. 2008;358:18-27.
18. Bello L, Gallucci M, Fava M, et al. Intraoperative subcortical language tract mapping guides surgical removal of gliomas involving speech areas. *Neurosurgery*. 2007;60:67-80 [discussion: 80–82].
19. Szelenyi A, Bello L, Duffau H, et al. Intraoperative electrical stimulation in awake craniotomy: methodological aspects of current practice. *Neurosurg Focus*. 2010;28:E7.
20. Duffau H. Lessons from brain mapping in surgery for low-grade glioma: insights into associations between tumour and brain plasticity. *Lancet Neurol*. 2005;4:476-486.
21. Sarubbo S, Le Bars E, Moritz-Gasser S, Duffau H. Complete recovery after surgical resection of left Wernicke's area in awake patient: a brain stimulation and functional MRI study. *Neurosurg Rev*. 2012;35:287-292 [discussion: 292].

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22. Ge J, Peng G, Lyu B, et al. Cross-language differences in the brain network subserving intelligible speech. *Proc Natl Acad Sci U S A*. 2015; 112:2972-2977.

23. Crinion JT, Green DW, Chung R, et al. Neuroanatomical markers of speaking Chinese. *Hum Brain Mapp*. 2009;30:4108-4115.

24. Jeong JW, Lee J, Kamson DO, Chugani HT, Juhasz C. Detection of hand and leg motor tract injury using novel diffusion tensor MRI tractography in children with central motor dysfunction. *Magn Reson Imaging*. 2015;33:895-902.

25. Gao B, Shen X, Shiroishi MS, et al. A pilot study of pre-operative motor dysfunction from gliomas in the region of corticospinal tract: evaluation with diffusion tensor imaging. *PLoS One*. 2017;12: e0182795.

26. Hendriks EJ, Habets EJJ, Taphoorn MJB, et al. Linking late cognitive outcome with glioma surgery location using resection cavity maps. *Hum Brain Mapp*. 2018;39:2064-2074.

27. Satoer D, Vork J, Visch-Brink E, Smits M, Dirven C, Vincent A. Cognitive functioning early after surgery of gliomas in eloquent areas. *J Neurosurg*. 2012;117:831-838.

28. Satoer D, Visch-Brink E, Smits M, et al. Long-term evaluation of cognition after glioma surgery in eloquent areas. *J Neurooncol*. 2014;116:153-160.

29. Anderson SI, Taylor R, Whittle IR. Mood disorders in patients after treatment for primary intracranial tumours. *Br J Neurosurg*. 1999;13:480-485.

30. Klein M, Duffau H, De Witt Hamer PC. Cognition and resective surgery for diffuse infiltrative glioma: an overview. *J Neurooncol*. 2012;108:309-318.

31. Litofsky NS, Farace E, Anderson F Jr, et al. Depression in patients with high-grade glioma: results of the Glioma Outcomes Project. *Neurosurgery*. 2004;54:358-366 [discussion: 366—357].

32. Mutschler I, Reinbold C, Wankerl J, Seifritz E, Ball T. Structural basis of empathy and the domain general region in the anterior insular cortex. *Front Hum Neurosci*. 2013;7:177.

33. Wiech K, Lin CS, Brodersen KH, Bingel U, Ploner M, Tracey I. Anterior insula integrates information about salience into perceptual decisions about pain. *J Neurosci*. 2010;30:16324-16331.

34. Mutschler I, Ball T, Wankerl J, Strigo IA. Pain and emotion in the insular cortex: evidence for functional reorganization in major depression. *Neurosci Lett*. 2012;520:204-209.

35. Shao J, Meng C, Tahmasian M, et al. Common and distinct changes of default mode and salience network in schizophrenia and major depression. *Brain Imaging Behav*. 2018;12:1708-1719.

36. Hamilton JP, Etkin A, Furman DJ, Lemus MG, Johnson RF, Gotlib IH. Functional neuroimaging of major depressive disorder: a meta-analysis and new integration of base line activation and neural response data. *Am J Psychiatry*. 2012;169:693-703.

37. Kaiser RH, Andrews-Hanna JR, Wager TD, Pizzagalli DA. Large-scale network dysfunction in major depressive disorder: a meta-analysis of resting-state functional connectivity. *JAMA Psychiatry*. 2015;72:603-611.

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