PRACTICAL APPLICATION OF NETWORKS IN NEUROSURGERY: COMBINED 3D PRINTING, NEURONAVIGATION, AND PRE-OPERATIVE SURGICAL PLANNING

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3 **Submission statement**

4 I certify that this manuscript is a unique submission and is not being considered for publication, in part or in full,
5 with any other source in any medium.

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ABSTRACT

Background: A plethora of cutting edge neuroimaging analyses have been developed and published yet they have not hitherto been realized as improvements in neurosurgical outcomes. In this paper we propose a novel interface between neuroimaging and neurosurgery for aiding translational research.

Objective: To describe a method for applying advanced neuroimaging and network analysis findings to pre-operative planning in neurosurgery, and illustrate its application through the presentation of two detailed case vignettes.

Methods: This interface comprises a combination of network visualization, 3D printing, and *ex vivo* neuronavigation to enable pre-operative planning according to functional neuroanatomy. Two clinical case vignettes are presented to illustrate this application in a prospective cohort design.

Results: The first case vignette describes a low grade glioma with potential language and executive function network involvement that underwent a successful complete resection of the lesion with preservation of network features. The second case describes a low grade glioma in a seemingly non-eloquent location that underwent a subtotal resection but demonstrated unexpected and significant impairment in executive function post-operatively that subsequently abated under long term follow-up. In both examples the neuroimaging and network data highlight the complexity of the surrounding functional neuroanatomy at the individual level, beyond that which can be perceived on standard structural sequences.

Conclusions: The described interface has widespread applications for translational research including pre-operative planning, neurosurgical training, and detailed patient counseling. A protocol for assessing its potential effectiveness and safety is proposed. Finally, recommendations for effective translation of findings from neuroimaging to neurosurgery are discussed, with the aim of making clinically meaningful improvements to neurosurgical practice.

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1 INTRODUCTION

2
3 The advent of MRI in the 1980s has created a wealth of neuroimaging data that describes cognition in health and
4 disease. Growth in neuroimaging data has been prolific, encompassing a vast array of techniques such as
5 mapping grey and white matter tissue characteristics, myelin maps, cortical and subcortical morphology, and
6 connectomics.¹ Pleasingly the field has been a leader in making multiple big data analyses freely available.²
7 With such a prolific, long-standing, and important field, one would expect the applications to neurosurgery to be
8 numerous and profound. However, this is not the case.

9
10 Reasons for this lack of translation from neuroimaging to neurosurgery are readily apparent. Publishing data on a
11 significant effect at the group level does not necessarily mean an analogous effect can be found or applied at the
12 individual level.³ Neurosurgical interventions are by necessity physical yet neuroimaging findings are essentially
13 visual and statistical, which necessitates an interface between the published data and operative application. A
14 meaningful change to neurosurgical interventions must also be defined *a priori*: that is, what does one wish to
15 change during surgery, how does neuroimaging satisfy this requirement, and will this make a difference to an
16 individual. Finally, there need to be suitable tools that provide neuroimaging data in a way that is accessible,
17 relevant, and easily interpretable in order to gain confidence in its ability to support clinical decisions.

18
19 We introduce a novel interface that enables the use of neuroimaging data for neurosurgical applications at the
20 individual patient level. This interface comprises: an advanced and customizable visualization platform of
21 individual neuroimaging data, in our case networks and connectomics; a 3D printout of an individual patient's
22 brain and tumor; and a trackable 'wand' used to navigate and display the pertinent network features on the
23 viewer for any specific point on the 3D brain. The interaction with the physical model is designed to provide a
24 realistic approximation of operating and allow the tracker to act as a virtual scalpel for modeling the predicted *in*
25 *silico* effects of surgery, and will be familiar to anyone having used a neuronavigation system. The main
26 differences are: application *ex vivo* in a simulation setting; navigation on a high-resolution cortical reconstruction
27 at high accuracy; and visualization of novel network and connectomic imaging data using our custom viewing
28 platform.

29
30 Given the quantity, complexity, and need for scientific validation of neuroimaging data, the natural timing to use
31 such an interface is pre-operatively in an exploratory manner. This will allow one to see the pertinent network
32 and connectomic features that could be relevant to the chosen surgical approach. Furthermore, it can be used to
33 plan out areas to investigate for either clinical or research testing *a priori*. To illustrate this application two case
34 vignettes will be presented to test and challenge contemporary surgical approaches in functional brain mapping
35 and neuro-oncology. Finally, a means to evaluate the potential of this method in a subsequent clinical trial will

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be described. We believe that such an interface will be key in bridging the aforementioned gap between scientific data and clinical applications.

METHODS

A summary of the interface and analysis pipeline is presented in figure 1.

1. Study Design

This study is a single centre prospective cohort design and was approved by the Local Regional Ethics Committee (protocol number 16/EE/0151). All participants provided written informed consent. Inclusion criteria were an MRI appearance of a non-enhancing diffuse tumor consistent with a low-grade glioma and planned to undergo awake brain surgery. Two patients were selected to form a prospective cohort that presented different clinical conundrums in order to identify potential variability in the chosen surgical approach that could be aided by the proposed pipeline. The proposed trial is registered at the Open Science Framework (OSF) managed by the Centre for Open Science (<https://osf.io/p5eg6>).

2. Imaging Data Acquisition

Our MRI data acquisition and processing are discussed in supplementary information 1. Note that the visualization interface has the flexibility to include a variety of neuroimaging analysis. The analyses presented herein are provided as examples to illustrate the potential for incorporating network and connectomic approaches.

3. Construction of 3D models

Cortical and tumor surface meshes are required to be in a suitable file formatted for 3D printing (figure 2). Standard pipelines for 3D printing using MRI data are available⁴⁻⁶, however these require modification when a tumor is present. All code for developing 3D brain and connectome models in patients with brain tumors has been made available online (http://github.com/jazzmanmike/braintumor_3D). Detailed instructions are presented in supplementary information 1.

4. Polhemus Interface and Neuronavigation

MATLAB 2016a (The MathWorks, Natick, Mass., USA) was used to create a Graphical User Interface (GUI) to control and interconnect the neuroimaging data with the Polhemus Patriot™ (Polhemus, Colchester, VT, USA) tracking system and the 3D printed brain. The printed brain was registered to the MPRAGE data. Static accuracy of the Polhemus tracking system is 2mm root mean square of the XYZ position. Note that this is a direct registration between the 3D and neuroimaging cortical surfaces thereby minimizing registration error. A

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correspondence between the space on the 3D brain and the structural MRI co-ordinate is thus created to view the relevant registered neuroimaging data using our custom viewer (figure 3).

5. Network Visualization

Once data have been processed and the 3D brain registered to the navigation software one can begin to view and interact with the chosen neuroimaging data (figure 4; Supplemental Digital Content Video 2 and 3, which illustrates interaction and outputs of the network visualization interface). Exemplar network visualizations include:

- Tractography visualized with MRTrix.⁷
- Resting state networks were binarized, converted to surface meshes, and labeled using cross-correlation of their surface topology with that of a series of canonical networks.⁸
- Connectomics and focused attack is performed by highlighting the top-weighted connections of a selected node as a means of capturing the functional associations that would be lost upon removal of that region.

RESULTS

Two participants were chosen for their non-trivial brain mapping requirements and potential variability in surgical approaches. Note that both patients were operated upon and managed according to their clinical data: the network interface was used for research purposes and not for clinical care.

Participant 1

A 22 year-old, left-handed female presented with recurrent nocturnal seizures subsequently controlled with levetiracetam. An MRI scan demonstrated a focal cortical non-enhancing tumor of the right middle and inferior frontal gyrus reported to likely represent a low-grade glioma (figure 5). Pre-operative neuropsychological assessment revealed only a mild reduction in scores on a single task of attention and scoring in the mild range for anxiety.

Awake brain surgery was performed with neuronavigation (StealthStation® S7® System, Medtronic, Inc, Louisville, CO, USA) and mapping goals of language but no sensitive areas were identified intra-operatively. Structural imaging revealed no evidence of residual disease on T2, FLAIR, or T1 pre and post-gadolinium sequences at three months post-operatively. Histology revealed a WHO grade I ganglioglioma. Follow-up management consisted of regular imaging and clinical assessment without further treatment. Post-operatively there was initially a period of fatigue that resolved within seven days. Formal neuropsychological assessment two weeks after surgery noted improved scores in mood and no new deficits. The patient was notably quick in responses and demonstrated sustained attention with no evidence of fatigue.

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Network data revealed an executive function network and putative language networks in close proximity to the tumor, particularly posteriorly. Both of these remained present at three months. Tractography revealed the majority of tracts to be deep to the lesion. Connectomics suggested network hubs adjacent to the tumor with modest intra and inter-hemispheric connectivity. Overall, the pre-operative network data suggested that this was a highly eloquent area both for language and executive function, possibly reflected by the subtle impairment in attention on neuropsychology testing. Complete resection of the lesion was performed without encroachment on these surrounding cortical networks or tracts, hence preserving connectome features and functional boundaries.

Pre-operative planning for this lesion requires consideration of an approach to identify language function. Task-based functional MRI or resting-state networks could be used to localize presumed language areas but these techniques do not exclude co-dominance or necessarily predict post-operative function. Our approach was to perform awake surgery with brain stimulation to maximize the potential of preserving language function. Furthermore we could identify peri-regional tracts (inferior fronto-occipital fasciculus), higher cognitive function (e.g. executive function) networks, and association cortex hubs surrounding the lesion that we would wish to study in detail intra-operatively to be sure of our functional boundaries. For research purposes one could identify putative language networks for further testing during surgery with advanced neuropsychology paradigms, or on assessment of executive function and attention.

Participant 2

A 29 year-old, right-handed male presented with a single nocturnal seizure and was placed on levetiracetam. An MRI scan demonstrated an infiltrating non-enhancing tumor of the left anterior superior frontal gyrus reported as a low-grade glioma (figure 6). Pre-operative neuropsychological assessment revealed minor reduction in scores with tests of story recall, word cognition, and verbal memory but otherwise high cognitive function.

Awake brain surgery was performed with neuronavigation and mapping goals of language and motor control but no sensitive areas were identified. Resection of the lesion was performed without complication with only a small possible residual of non-enhancing tumor at the deep margins. Histology revealed a WHO grade II astrocytoma (IDH-1 mutated, ATRX-mutated, 1p/19q co-deletion negative). Follow-up management consisted of regular imaging and clinical assessment without further treatment.

Post-operatively there was a period of initial fatigue that had resolved within five days. Neuropsychological examination initially revealed a mixed picture at 2 weeks post-operatively. There were improvements in initiation and in a task of non-verbal memory without a timed component. However there were also lower scores in design learning, design recall, immediate verbal recall, list recognition, inhibition timing, and inhibition scores. By 12 months his performance had returned to be consistent with his pre-surgical baseline.

Network Simulation

Network data revealed multiple typically demarcated executive function and attention networks in the vicinity of the tumor. Tractography demonstrated significant intra-hemispheric local and long-range connectivity immediately adjacent to the tumor. Post-operatively resting state network topology and connectivity was markedly reduced. Connectomics revealed a similar picture with hub reorganization to the contralateral homologous region from the tumor and a reduction in connectivity of adjacent hubs particularly involving intra-hemispheric connections. Overall these disrupted connectome features are consistent with on-going clinical recovery and in keeping with the neuropsychological examination. Notably major adjacent tracts such as the superior longitudinal fasciculus were preserved.

In terms of pre-operative planning, surgical approaches to this lesion would largely be concerned with avoiding the supplementary motor area (SMA) more posteriorly. In our case we were also interested in networks the adjacent tracts such as the frontal-aslant and fronto-striatal tracts, which highlights the importance of not just mapping the cortex but also the deep boundaries in the white matter. From a research perspective, numerous networks and hubs can be identified adjacent to the lesion that one might suppose to be involved in executive function, which could be used as a basis for more extensive intra-operative testing or rehabilitation peri-op.

DISCUSSION

We presented a rapid, cost-effective, and generalizable interface for application of neuroimaging data with neurosurgery. Benefits of the approach include its customizability and generalizability to multiple forms of neuroimaging data. Furthermore it could be expanded to the intra-operative situation, used pre- and post-operatively for educational purposes, as well as in clinic to counsel patients about the proposed surgery.

The case examples are presented to illustrate the application of neuroimaging data to neurosurgery and in particular where it could make a difference in clinical practice. The first participant had a right inferior frontal low-grade glioma that was complicated by the patient being left-handed and potential involvement of language and executive function networks. A surgical approach that focused on complete resection while also being mindful of preserving this surrounding highly eloquent brain corresponded with the excellent neuropsychological outcome with improvement in many domains, as well as largely untouched brain network imaging results. The second participant had a left frontal low-grade glioma just anterior to the SMA which involved several higher cognitive function networks well recognized to potentially have profound, albeit often temporary, post-operative deficits. In this instance additional executive function networks were found adjacent to the tumor, with transient impairment in the corresponding networking imaging results that corresponded with the long-term neuropsychological recovery. One could predict that a more aggressive strategy here would have potentially disastrous long-term consequences.

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The value of the interface in both these circumstance is in further delineating the functional and structural anatomy before performing the surgery. That is, the interface is not necessarily designed to change actions during surgery *per se*, but rather it is designed to change ones approach to surgery (for example awake or asleep) and consequently the resection that is performed (for example conservative, total, or supra-total resection of the lesion). This paper provides the necessary premise for understanding this approach, while we have developed plans to test its effectiveness in a subsequent cohort study.

Using neuroimaging at the individual level highlights several crucial methodological issues that need to be resolved. Regarding resting state networks, there are issues regarding naming of individual networks, thresholding, and viewing multiple networks in a convenient manner (both the cases viewed a single network but this ignored other potential networks in the vicinity). Tractography has its own set of issues that are well described in the literature including resolving complex tract trajectories, identifying long-range tracts, and determining the site of cortical termination.⁹ Additional issues include determining the function of an individual tract, and predicting the functional sequel to tract disruption in terms of plasticity (networks can restore structural function through degeneracy and redundancy without requiring new tracts to be generated, for example). Issues with connectomics essentially relate to visualization and interpretation. Connectomes, particularly functional, often contain many more connections than can be easily viewed, and the effect on network measures of *in vivo* lesioning is not readily apparent. Finally, brain shift itself is an important problem if network data is to be used intra-operatively. This problem in itself should be tractable to solutions involving re-registration based on surface morphology intra-operatively or using suitably trained surface deformation models. However it may be that neuroimaging data are best used pre-operatively for planning purposes, and that additional navigation intra-operatively is likely to obfuscate accurate surgery. Despite these limitation the data provides a valuable additional tier of information to neurosurgeons, when interpreted appropriately.

Prospectively and objectively assessing the effectiveness and safety of any new intervention is of paramount importance, especially with regards to new surgical technology. With this interface there are clearly multiple steps that require evaluation, such as the visualization of the data, the validity of the data, and how it affects the surgical approach. Clearly with such a complex intervention clinical trials should be designed towards a process of repeated assessment and refinement, analogous to beta testing in software design, rather than one single definitive test. Therefore in the first instance we propose to assess how individual surgeons approach the resection of lesions in individual patients, and how this can be affected by 3D printing and our interface. A pre-print of our planned questionnaire, study design, and statistical analysis is available in supplementary information 4 and 5 as well as being registered online (<https://osf.io/p5eg6>).

CONCLUSIONS

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Ultimately the challenge is to translate basic science research for real patient benefit. This requires appreciation of available approaches and their meaning, data to highlight their usefulness, and a means of translating studies from interesting papers to a practical application at the individual patient level. The interface described within is but one possible solution, and it is proposed partly to stimulate research and open the door to further studies rather than represent the single best solution. Strengths include the physical interaction, portability, cost effectiveness, and flexibility. Potential roles are proposed in pre-surgical planning, intra-operative mapping, academic research, training, and patient counseling. Further characterization of its role in pre-operative planning, optimal visualization of data, and characterization of what scenarios it is of most benefit in is required. It is hoped that presenting this interface will generate discussion and engagement with the neurosurgical community, which will be essential in translating neuroimaging data to any discernable benefit to patient care.

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DISCLOSURES

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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<https://github.com/miykael/3dprintyourbrain>

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FIGURE LEGENDS

Figure 1: Analysis Pipeline

To perform network navigation with the interface described herein, it is first necessary to acquire MRI data, either using the sequences described in the paper or others. Subsequently this data is processed and network analysis performed that will be used for later visualization. The processed structural data is used to create the 3D printed model that forms the core physical interaction point of the interface. Subsequently the interface between the tracker system, for example the Polhemus Patriot™ system (Polhemus, Colchester, VT, USA), and a personal computer is initiated. Registration of the 3D brain to the network data to be visualized is then performed. Finally, the series of co-ordinates from navigation is used to display the network data.

Figure 2: 3D Printing

Examples of 3D printed brain models that can be used for network navigation. Each column refers to a specific participant. In this paper participant one is on the left and participant two is on the right. The top row represents a 3D printed grey matter / pial surface rendering with the tumor volume colored in red. The lower row represents an example connectome with nodes overlapping the tumor in red.

Figure 3: Network Interface

Practical visualization of the network simulation setup. The 3D brains from each participant are seen with tracker wand adjacent, electromagnetic field generator in black, connected to a personal computer with network visualization software running.

Figure 4: Network Simulation Visualization

A screenshot of the network simulation software. This offers multimodal network representations to be viewed and coupled to either a tracker wand, neuronavigation interface, or using the touchscreen. In this example four

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views are offered: standard structural MRI (sagittal, axial and coronal axes); tractography; resting state networks on a cortical mesh; and focal lesioning of connectomic data.

Figure 5: Participant 1 Network Data

Top row: pre-operative data. Lower row: corresponding data from month three follow-up. Images are (from left to right, both rows): FLAIR, resting state networks in MNI space with underlying MPAGE, tractography, and virtual lesioning of connectomic data.

Figure 6: Participant 2 Network Data

Top row: pre-operative data. Lower row: corresponding data from month three follow-up. Images are (from left to right, both rows): FLAIR, resting state networks in MNI space with underlying MPAGE, tractography, and virtual lesioning of connectomic data.

Supplemental Digital Content 1. MRI acquisition and processing

Details of MRI sequence parameters and image processing.

Supplemental Digital Content 2. Network Simulation Setup and Interaction [video].

Video that illustrates the setup and interaction with the network visualization interface.

Supplemental Digital Content 3. Network Simulation Visualization [video].

Video that illustrates the outputs of the network visualization interface.

Supplemental Digital Content 4. Proposed assessment protocol

Proposed study protocol for assessing the effectiveness of the network simulation approach.

Supplemental Digital Content 5: Example cases.

A selection of 5 case vignettes which have been prepared to test the effectiveness of the network simulation approach. For each case the clinical details, expected questions that will be generated, and predicted effects on surgical approach and extent of resection are described.

Supplementary Information 1: Methods**Neuroimaging Data Acquisition**

MRI data were acquired using a Siemens Magnetom Prisma-fit 3 Tesla MRI scanner and 16-channel receive-only head coil (Siemens AG, Erlangen, Germany). Total acquisition time was: MPAGE – 9 minutes and 14 seconds, rs-fMRI – 9 minutes and 10 seconds; NODDI – 15 minutes and 19 seconds.

Structural

Anatomical images were acquired using a T1-weighted magnetization prepared rapid gradient echo (MPAGE) sequence (FOV 256mm x 240mm x 176mm; voxel size 1mm isotropic; TR 2300ms; TE 2.98ms; flip angle 9 degrees).

rs-fMRI

Functional images were acquired using single-echo echo planar imaging (EPI) sequence (FOV 192mm x 192mm x 112mm; voxel size 2mm isotropic; TR 1060ms; TE 30ms; flip angle 74 degrees) generating 512 three-dimensional volumes of the supratentorial compartment.

NODDI

Diffusion-weighted images were acquired using Neurite Orientation Dispersion and Density Imaging (NODDI) with two different B values (800 & 2000) and both 32 and 64 directions (FOV 240mm x 240mm x 150mm; voxel size 2.5mm isotropic; TR 8200ms; TE 95ms) and GRAPPA acceleration.¹⁵

Neuroimaging Data Processing**Structural**

Advanced Normalization Tools (ANTs) cortical thickness pipelines were used for structural analysis (<https://stnava.github.io>). Data were intensity normalized, brain extracted, and nonlinearly mapped to the template of the Montreal Neurological Institute (MNI152) at 2mm resolution using symmetrical diffeomorphic registration. A hand drawn mask of the tumor was used to exclude this region from the cost function during registration.

rs-fMRI

Resting state networks were based on Independent Component Analysis (ICA) performed with MELODIC^{1,2} with de-noising using FIX with training specific to this dataset^{3,4}. Data were pre-processed with rigid body motion correction, coarse brain extraction, normalized by a single scaling factor, smoothing to 5mm fixed width half maximum, and highpass temporal filtering. Linear registration (6 degrees of freedom) was performed to the corresponding MPAGE using ANTs.

Connectomes were constructed in functional space using an anatomically principled template subsequently random subdivided into 318 symmetrical equally-sized (500mm^2) cortical and 16 subcortical regions.⁵ Links were determined by the Pearson correlations of processed rs-fMRI time series.

NODDI

Whole brain tractography was performed with BedPostX and ProbTrackX (FSL -FMRIB Software Library version 5.0, www.fsl.fmrib.ox.ac.uk). Complementarily, direction-encoded colored tractograms were generated for visualization purposes using constrained spherical deconvolution and probabilistic streamlines algorithm implemented in MRTrix.⁶ Connectomes were constructed in diffusion space using the same template as for rs-fMRI with weighted links determined by the number of streamlines between parcels.

Construction of 3D models

Cortical surface reconstructions, a necessary first step in generating a cortical mesh, are based on identifying the gray-white matter interface: the presence of a lesion can obscure this boundary and cause standard algorithms to fail. To obviate this issue the tumor region was removed and replaced with homologous cortex to reconstitute the gray-white matter interface in a process known as enantiomorphic filling.^{7,8}

Tumor segmentation masks were initially drawn manually using FSL (FMRIB Software Library version 5.0, www.fsl.fmrib.ox.ac.uk) following which the subsequent mask was refined using semi-automated pipelines (Unified Segmentation with Lesion toolbox, <https://github.com/CyclotronResearchCentre/USwithLesion>, unpublished observations). Brain extraction of the MPAGE volume is performed using a template-based method with ANTs.⁹ The extracted brain then underwent enantiomorphic filling of the tumor region following a cortical reconstruction using FreeSurfer (version 6.0 for Linux, www.surfer.nmr.mgh.harvard.edu).¹⁰ Cortical surface ribbons were converted to a surface mesh and stereolithography files then viewed on MeshLab 2016 (IST-CNR, www.github.com/cnr-isti-vclab/meshlab)¹¹ where they underwent final pre-processing with scale dependent Laplacian smoothing. Tumor masks were tessellated to create a surface mesh then processed in the same manner as cortical surface ribbons.

Resulting stereolithography files were scaled and printed at Addenbrooke's Media Studio (Addenbrooke's Hospital, Cambridge, UK) for 3D Printing (process: 3D ColorJet Printing Technology, machine specification: ProJet 660 Pro (3D Systems®, Rock Hill, SC, USA), materials specification: VisiJet® PXL™ (plaster powder, 3D Systems®, Rock Hill, SC, USA) and ColorBond™ (cyanoacrylate) infiltrant (3D Systems®, Rock Hill, SC, USA), machine parameters and settings: full resolution full color print mode).

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NETWORK SIMULATION SOFTWARE BETA-TEST: METHODS AND ANALYSIS PRE-PRINT

Hypotheses

What is the variability in surgical approaches to the resection of low grade gliomas?

What potential is there to alter a planned surgical approach based on additional information?

How does information from 3D models and network data affect neurosurgical planning?

Study Design

Neurosurgeons are asked to plan their surgical approach on 5 distinct clinical scenarios involving low grade gliomas. For each scenario they will be asked the same questions in 3 stages:

Stage 1: Plan resection based on standard clinical MRI scans: 'normal' approach

Stage 2: Plan resection based on standard clinical MRI scans plus 3D model

Stage 3: Plan resection based on standard clinical MRI scans plus 3D model plus network simulation software (including Polhemus wand interface)

Questions

At each stage the same questions will be asked:

Stage 1: 'Normal' MRI

1. What is the predicted extent of resection?
2. What would be your surgical approach i.e. awake/asleep, advanced imaging (task fMRI, tractography, other), ECoG

Additionally:

- What functional questions do you wish to know?

Stage 2: 3D Model

1. What is the predicted extent of resection?
2. What would be your surgical approach i.e. awake/asleep, advanced imaging (task fMRI, tractography, other), ECoG

Additionally:

- What would be your margins?
- What functional questions do you wish to know?
- Would you resect more or less than the tumour?

Additionally for 3D:

- Does the 3D model help with planning?
- Would you use it intra-operatively?

Stage 3: 3D Model plus network visualization interface

1. What is the predicted extent of resection?
2. What would be your surgical approach i.e. awake/asleep, advanced imaging (task fMRI, tractography, other), ECoG

Additionally:

- What would be your margins?
- What functional questions do you wish to know?
- Would you resect more or less than the tumour?

For 3D & network visualization:

- Would you use it intra-operatively?
- What data was useful?
- What data wasn't?
- Was the display helpful?

Scenarios

A repertoire of 5 example scenarios have been prepared (see Table 1, Supplemental Content, which illustrates the scenario, expected questions that will be generated, and predicted effects on surgical approach and extent of resection). Note that the first two cases have been described in detail in the main manuscript.

Statistical Analysis

Paired contingency test analysis (McNemar's test)

Correction (Bonferroni) for multiple comparisons

Predicted effect size:

- 50% of surgeons change their operative approach based on additional information (3D *or* 3D + network visualization)
- Change in approach defined as different aim (subtotal versus total versus supratotal resection) or different method (awake versus asleep or additional monitoring / imaging intra / peri-op)

Power calculation:

- Single paired study group
- Binomial outcome (change in approach)
- Varies with initial
- Alpha = 0.05
- Power = 80%
- Sample size = 28
- Subgroups: analysis of different aims and methods separately (including subgroups of each e.g. change from awake to asleep only)

Scenario	Tumour location	Question for 3D/Network Data	Predicted effect on surgical approach	Predicted effect on extent of resection
1. Un-resectable tumour	Insula glioma	Will this become more resectable?	Nil (awake)	More extensive but subtotal
2. Eloquent: motor	Pre-central gyrus	Will there be a move to a more extensive resection?	Nil (awake)	More extensive but subtotal
3. Eloquent: language	Right inferior frontal (left handed patient)	Will there be more concern over functional boundaries?	Move to awake mapping from asleep	More extensive / supra-marginal
4. SMA syndrome	Left SMA	Will there be a change to the surgical approach?	Move to awake mapping from asleep	More conservative
5. 'Non'-eloquent	Left frontal-pole	Change in consideration of eloquence?	Move to awake mapping from asleep	More conservative

Info
Cortical Region: RH rostralmiddlefrontal_part5

Change to Wand Control