Advanced Neuroimaging and Pediatric Epilepsy Surgery

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Neuroimaging in epilepsy surgery

Epilepsy, a common chronic brain disorder characterized by recurrent unprovoked seizures, usually has onset during childhood. Worldwide, epilepsy affects 10.5 million children and represents about a quarter of the global epilepsy population [1]. At least 50% of epilepsy during childhood is of focal onset, and up to 30% of children with focal epilepsy have seizures that are incompletely controlled on medications [2]. Epilepsy surgery offers some of these children the opportunity for seizure freedom, improvements in development and overall better quality of life for them and their family [3].

Advanced multi-modal magnetic resonance imaging (MRI) techniques are pivotal to comprehensive presurgical evaluation in children [4]. These advanced imaging techniques contribute to lesion identification; localization of the seizure focus, with concordant clinical and electrophysiological information; lateralisation of the language dominant cerebral hemisphere [5]; and localization of functional cortical and subcortical brain regions subserving movement, memory, language and visual function. Advanced multi-modal MRI has the potential to simplify the patient’s presurgical workup, obviate the need for intracranial EEG monitoring and electrical stimulation, improve postoperative seizure outcome, and avoid or minimize postoperative neurological deficits.

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Table 1: MR acquisition parameters for DWI, fMRI, and fMRI sequences.

<table>
<thead>
<tr>
<th>TR</th>
<th>TE</th>
<th>FOV</th>
<th>Matrix</th>
<th>Slice</th>
<th>Grappa</th>
<th>SMS</th>
<th>B₀ Shim</th>
<th>Ref Scan</th>
<th>RF Mode</th>
<th>Gradient</th>
<th>ESP</th>
<th>BW</th>
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<td>4000</td>
<td>78 ms</td>
<td>244</td>
<td>122 100%</td>
<td>2 mm 2</td>
<td>2</td>
<td>Adv</td>
<td>Gre/Sep</td>
<td>Normal Performnace</td>
<td>0.58 ms</td>
<td>2276 Hz/Px</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Multi-Shell DWI MAGNETOM Prisma syngo MR E11C 32-channel Head Coil

| 1500| 30 ms| 255 | 104 100% | 2.5 mm 2 | 3 | Adv | FLEET | Normal Performnace | 0.5 ms | 2404 Hz/Px |

fMRI Language Task MAGNETOM Prisma MB Acquisition syngo MR E11C 32-channel Head Coil

| 1500| 30 ms| 255 | 104 100% | 2.5 mm 2 | 3 | Adv | FLEET | Normal Performnace | 0.5 ms | 2404 Hz/Px |

Resting State MAGNETOM Prisma MB Acquisition syngo MR E11C 32-channel Head Coil

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1 MR scanning has not been established as safe for imaging fetuses and infants less than two years of age. The responsible physician must evaluate the benefits of the MR examination compared to those of other imaging procedures. Note: This disclaimer does not represent the opinion of the authors.
Diffusion MRI tractography – Limitations of Diffusion Tensor Imaging (DTI)

Diffusion MRI tractography is a post-processing imaging technique that generates virtual reconstructions of the anatomy of brain nerve fibre tracts, also known as white matter tracts (WMTs) [6, 7]. Accuracy of the tractography reconstruction is paramount in neurosurgery because surgical injury to the WMTs or their blood supply can lead to permanent neurological deficits [8–10]. MRI data can be coregistered and overlaid on a live view of the patient’s brain during surgery, using image-guided navigation software. Preoperative tractography combined with the intraoperative live view of the patient, provide important information to the neurosurgeon to plan the optimal surgical approach to minimize injury to surrounding healthy brain structures.

The tractography techniques adopted in neurosurgery traditionally involve diffusion tensor imaging (DTI) data acquisition and a deterministic tractography algorithm, but this approach is unable to accurately model diffusion over crossing fibre regions [11, 12], present in up to 90% of the cerebral white matter (WM) [13]. State-of-the-art methods are available that improve WMT modelling, with advances in diffusion MRI data acquisition, improved tracking algorithms, and better methods for image-based tract reconstructions. Modern tractography techniques incorporate high angular resolution diffusion imaging (HARDI) data acquisition and probabilistic fibre tracking [14] based on the constrained spherical deconvolution (CSD) crossing fibre models [15, 16], improving tractography results in ways that have a significant impact on surgical planning and intraoperative image-guidance.

More recent advances in tractography include multi-shell and multi-band diffusion acquisitions. Multi-shell diffusion imaging acquires low, intermediate and high b-value diffusion data in one sitting, producing diffusion propagation maps that are more specific to the WM tissue domain [17]. This is termed the multi-shell multi-tissue-CSD (MSMT-CSD) technique. MSMT-CSD improves the accuracy of fibre-orientation distribution (FOD) estimation in WM regions over the grey-white matter tissue interface and removes noisy isotropic voxels that belong to the cerebrospinal fluid space, thereby improving further the anatomical accuracy of the tractography reconstruction (Fig. 1). Multi-band or simultaneous multi-slice acquisition schemes reduce the time needed to acquire multi-shell diffusion data within a clinically acceptable timeframe [18, 19].

Diffusion MRI tractography at the Royal Children’s Hospital, Melbourne

Since 2012, advanced tractography reconstructions using HARDI data acquisition and based on CSD crossing-fibre modelling and probabilistic tracking have been used for preoperative planning for epilepsy surgery at the Royal Children’s Hospital, Melbourne, Australia. The introduction of multi-band, multi-shell DWI acquisition in 2016 further improved the anatomical accuracy of our tractography reconstructions. Combined with clinical expertise and other imaging and electrophysiological modalities, we believe our clinical tractography program has contributed to improved seizure and functional outcomes in children undergoing epilepsy surgery. In this article we present the neuroimaging data for three children in whom tractography played a role in pre-surgical planning for their epilepsy surgery.

MR protocol at the Royal Children’s Hospital, Melbourne

Our early implementation of multi-band diffusion sequences and SMS TSE into our comprehensive epilepsy protocol utilized MAGNETOM Trio / MAGNETOM Verio syngo MR B17 software and resulted in a significant improvement in our diagnostic imaging protocols (spatial resolution, reduction in scan times and integration of advanced image analysis). Prior to implementing these sequences into clinical practice we undertook comprehensive comparative studies in volunteers using conventional and multi-band acquisitions plus analysis pipeline verification. The comparative studies looked at the optimization of protocols for 3T [20–22], variations in tSNR that could affect analysis of resting state data [23], interslice artefacts [24, 25], effects of patient movement during the ACS acquisition [26, 27] and how far we could push the multi-band factor on our systems [28–30]. Our initial protocols (DWI, fMRI and rfMRI) have been transitioned through to our current systems (MAGNETOM Prisma syngo MR E11C and Biograph mMR syngo MR E11P) with modifications to the imaging parameters, notably multi-band factors and spatial resolution (Table 1). Multi-shell acquisitions are acquired using 3 separate scans (Monopolar diffusion scheme; b = 3000 s/mm², 69 dir including 5 b = 0, b = 2000 s/mm², 50 dir including 5 b = 0 and b = 1000 s/mm², 30 dir including 5 b = 0) using a custom vector file.
Advanced diffusion MRI white matter modelling and tractography reconstruction in a patient with focal drug refractory epilepsy referable to a developmental brain tumor located in the left fusiform gyrus (white dashed circle, (1A) T1-weighted image). Multi-band, multi-shell diffusion data acquired using a 3T MAGNETOM Prisma Siemens scanner, was used to reconstruct the optic radiation tractography (yellow color in 1B) closely abutting the tumor. The reconstructed tractography closely resemble cadaveric fibre dissection (blue arrows in 1C); taken from Ludwig & Klinger’s atlas, 1956.

(1D) shows the multi-shell multi-tissue-constrain spherical deconvolution (MSMT-CSD) framework improves tissue specificity of the diffusion mask, and the accuracy of corresponding fibre orientation distribution (FOD) estimations, than the traditional approach of using single-shell single-tissue-CSD (SSST-CSD). Combinations of these features improved anatomical accuracy of the tractography output. CSF = cerebrospinal fluid; GM = gray matter; WM = white matter.
Case 1
In this case, we present neuroimaging data from an adolescent with temporal lobe epilepsy. Seizure onset was at two years of age, with seizures from wake and sleep characterized by staring, confusion, speech difficulties and sometimes convulsing. The seizures were refractory to numerous antiepileptic medications. MRI showed a long bottom-of-sulcus focal cortical dysplasia in the left superior temporal sulcus, which merged into the sylvian fissure at the lateral convexity. The dysplasia was characterized by cortical thickening and grey-white blurring on T1-weighted MPR images, subcortical signal hyperintensity on FLAIR and T2-weighted images, and hypometabolism on FDG-PET images. Also associated with the dysplasia was an unusual transmantle band leading to a periventricular nodule in the left trigone.

2A
FLAIR image showing an extensive focal cortical dysplasia in the left superior temporal sulcus (2A) with a transmantle band and periventricular nodule at the trigone (2B).

2B

3 3D surface-rendered, co-registered T1-weighted MRI and FDG-PET with oblique slice showing focal hypometabolism in the depth of the cortical dysplasia which involved the left superior temporal sulcus at the depth and the sylvian fissure at the lateral convexity superior temporal sulcus.

4 Axial slices from language fMRI with a verb generation task showing left medial frontal, inferior frontal and inferior temporal BOLD activation. The surface-rendered 3D image shows the atypical localization of temporal activation in the inferior temporal gyrus.
Functional MRI with a visually-presented verb generation paradigm [31] showed left lateralization of language activation. Typical distribution of frontal activation was observed in the posterior-medial frontal region and frontal operculum; however, temporal activation was somewhat atypical, with the greatest activation in the inferior (as opposed to superior) temporal gyrus. No BOLD activation was seen in the dysplasia.

Probabilistic tractography was performed on HARDI data [15, 16, 32] to localize the superior longitudinal fasciculus (SLF) and the optic radiations (OR), in particular their relationship to the deeper components of the dysplasia. The temporal projections of the left SLF travelled immediately medial to the depth of the dysplastic superior temporal sulcus. The majority of the cortical terminations of the left SLF were in the inferior temporal gyrus, which corresponded with location of the temporal BOLD activation. The left OR travelled through and around the transmantle band in the WM between the depth of the dysplasia and the periventricular nodule.

The functional and structural imaging therefore showed the extent of the dysplasia, the likely absence of function in the dysplasia, the proximity of language cortex and WM pathways to the superficial and deeper components of the dysplasia, and the passage of the transmantle component of the dysplasia through the visual pathways. The epilepsy surgery team could conceivably proceed with knowledge of the operative risks and without need for additional electrical stimulation mapping.
Case 2

This patient was a primary school aged child with a brief history of focal seizures with prominent confusion and aphasia. They occurred at weekly frequency, despite several antiepileptic medications being trialled. MRI revealed a lesion in the left temporal lobe laterally and posteriorly, involving grey and white matter and filling a gyrus. The lesion was believed to be a low-grade glioma, rather than a focal cortical dysplasia or developmental tumor. Minor growth was seen on serial imaging over six months.

On functional MRI using a visually-presented verb generation task [31], language was left lateralized. There was language activation in cortex medial to and surrounding the lesion. Probabilistic tractography was performed on HARDI data [15, 16, 32] to localize the superior longitudinal fasciculus (SLF). The terminations of the SLF tracts were in the cortex and WM abutting the lesion, where BOLD activation was seen on fMRI. Optic radiation (OR) tractography showed visual pathways travelled deeper to the SLF. The functional imaging indicated that surgery would need to be a conservative lesionectomy, sparing superficial and deep language cortex and pathways.

7 Appearance of left temporal lesion on T2-weighted coronal image.
8 Language BOLD activation in left hemisphere relative to temporal lesion (crosshair).
9 3D renders of the left hemisphere showing language BOLD activation (9A) and SLF terminations (9B) relative to the temporal lesion.
10 3D tractography showing the location of the SLF (blue) and OR (green) in relation to the lesion (yellow).
Case 3
Here we present neuroimaging data from a child with recent-onset of seizures secondary to a left medial temporal-occipital tumour. Seizures were characterized by behavioural arrest, head and eye deviation and repetitive hand movements, followed by brief nonsensical speech. MRI showed a multi-cystic, cortically-based and contrast-enhancing tumor in the left fusiform gyrus, abutting the parahippocampal gyrus and calcarine fissure. The tumor had mixed MRI features of a DNET and PCA and showed slight change in enhancement and size on serial imaging. Left language dominance was established with functional MRI utilizing verb generation and verbal fluency paradigms [31]. Additionally, it revealed prominent BOLD activation in the posterior-basal temporal lobe, just lateral to the tumor.

Probabilistic tractography was performed on HARDI data [15, 16, 32] to localize the SLF and OR pathways. It revealed that the tumor was encircled by visual and language pathways, indicating significant risk of deficits in cognition, language, verbal memory and peripheral vision with attempted resection. However, with the aid of neuronavigation, preoperative simulated surgery using the detailed tractography data, and intraoperative MRI (IMRIS), surgery was performed with the impression of complete resection and no neurological deficits. Postoperative imaging and assessments are pending.

11A Appearance of left medial temporal-occipital tumour on T2-weighted axial (11A) and coronal (11B) image.

12 Lateral and oblique cut-aways showing the basal temporal language BOLD (noun verb = orange; verbal fluency = blue) overlying the tumor.
Tractography in relation to the tumor (brown). OR = optic radiation, SLF-AI = anterior indirect segment of superior longitudinal fasciculus, SLF-DS = direct segment of superior longitudinal fasciculus, SLF-PI = posterior indirect segment of superior longitudinal fasciculus, ILF = inferior longitudinal fasciculus, IFOF = inferior fronto-occipital fasciculus, UF = uncinate fasciculus.

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References


