Meyer's loop tractography for image-guided surgery depends on imaging protocol and hardware

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\textbf{Abstract}

Introduction: Surgical resection is an effective treatment for temporal lobe epilepsy but can result in visual field defects. This could be minimized if surgeons knew the exact location of the anterior part of the optic radiation (OR), the Meyer's loop. To this end, there is increasing prevalence of image-guided surgery using diffusion MRI tractography. Despite considerable effort in developing analysis methods, a wide discrepancy in Meyer's loop reconstructions is observed in the literature. Moreover, the impact of differences in image acquisition on Meyer's loop tractography remains unclear. Here, while employing the same state-of-the-art analysis protocol, we explored the extent to which variance in data acquisition leads to variance in OR reconstruction.

Methods: Diffusion MRI data were acquired for the same thirteen healthy subjects using standard and state-of-the-art protocols on three scanners with different maximum gradient amplitudes (MGA): Siemens Connectom (MGA = 300 mT/m); Siemens Prisma (MGA = 80 mT/m) and GE Excite-HD (MGA = 40 mT/m). Meyer's loop was reconstructed on all subjects and its distance to the temporal pole (ML-TP) was compared across protocols.

Results: A significant effect of data acquisition on the ML-TP distance was observed between protocols ($p < .01$ to $0.0001$). The biggest inter-acquisition discrepancy for the same subject across different protocols was 16.5 mm (mean: 9.4 mm, range: 3.7–16.5 mm).

Conclusion: We showed that variance in data acquisition leads to substantive variance in OR tractography. This has direct implications for neurosurgical planning, where part of the OR is at risk due to an under-estimation of its location using conventional acquisition protocols.

1. Introduction

Temporal lobe epilepsy (TLE) seizures originate in the temporal lobe and may be focal, localised to discrete cortical or subcortical regions within the temporal lobe, or may spread to other parts of the brain. An effective treatment for TLE consists of performing anterior temporal lobe resection (ATLR), often combined with amygdalohippocampectomy (Wiebe et al., 2001). One approach, the trans-middle temporal lobe resection (ATLR), enters through the trans-mid temporal gyrus approach (or transcortical), enters through the trans-middle temporal gyrus. A second approach, the sub-temporal approach, is less complex but can cause significant damage to the neocortex. A third, and most technically difficult approach, is one where the neurosurgeon has to access the brain though the transthyssian fissure. This technique reduces displacement of brain tissues but carries a greater risk of vascular complications (Bandt et al., 2013; Kovanda et al., 2014).

All three surgical approaches can result in visual field deficits (VFDs) in more than half of the patients undergoing the procedures, reducing the quality of life of these patients (Pathak-Ray et al., 2002). This is due to the transection of the optic radiation (OR), a white matter (WM) fibre bundle of utmost importance, responsible for transmitting visual information between the lateral geniculate nucleus (LGN) and the visual cortex (Ebeling and Reulen, 1988; Rubino et al., 2005; Winston et al., 2012). Meyer's loop is a section of the OR that projects most anteriorly, with a sharp backwards bend (Chamberland et al., 2017; Ebeling and Reulen, 1988; Goga and Ture, 2015). The extent and angulation to which the Meyer's loop fans out anteriorly is known to vary between subjects. From a neurosurgical perspective, it behooves us to pay particular attention to the 3D trajectory of the OR in order to reduce the risk of inducing VFDs. Knowing the exact location of the OR, and more specifically of the Meyer's loop, is crucial information that may help reduce morbidity for patients undergoing ATLR. Therefore, subject-specific information on the distance between the most anterior tip of the Meyer's loop and the temporal pole (TP), also referred to as the ML-TP distance (Fig. 1, Table 1), could greatly aid surgeons in preparation for such intervention, and lead to improved patient outcome. However, the anterior extent of Meyer's loop is 1) often located within the resection area; 2) known to vary between subjects (Goga and Ture, 2015) and 3) invisible on conventional MRI techniques.

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the acquisition time. However, recent advances in hardware have led to dramatic improvements in data quality and reductions in scan duration (Sotiropoulos et al., 2013). Stronger magnetic field gradients not only allow higher SNR at high b-values, but also provide better spatial resolution. Concomitantly, achieving better SNR and/or angular resolution allows better estimation of complex fibre orientations (Sotiropoulos and Zalesky, 2017; Tournier et al., 2011). In addition, multiple b-values allow more accurate estimation of partial volume effects, a necessity for achieving better estimation of WM directions (Jeurissen et al., 2014), which in turn will directly impact the results of tractography (Maier-Hein et al., 2017).

In this paper, we hypothesize that a more complete Meyer’s loop reconstruction can be achieved by using state-of-the-art (SoA) hardware and analysis techniques. To this end, we compare the ML-TP distance derived from tractography of the same thirteen subjects (healthy controls) acquired on three different scanners, using a mixture of five standard (Std) and SoA protocols.

2. Methods

2.1. Data acquisition

Written informed consent was given by all subjects. Meyer’s loop reconstructions were evaluated on a dedicated dataset (Tax et al., 2018) of the same 13 subjects (labelled from A to M) acquired on three different 3T scanners with different maximum gradient amplitudes (MGA): Siemens Connectom (MGA = 300 mT/m); Siemens Prisma (MGA = 80 mT/m) and GE Excite-HD (MGA = 40 mT/m) using Std and SoA acquisition protocols, with the latter having higher spatial and angular resolution. Acquisition parameters for all protocols are summarised in Table 2. A T1-weighted 1 mm isotropic MPRAGE image was acquired for each subject and scan for anatomical reference.

2.2. Data pre-processing

Eddy current distortion- and motion correction was performed using

Since the OR cannot be identified visually during surgery, substantial effort has been exerted in obtaining an accurate localization of the OR using tractography derived from dMRI (for review, see (Benjamin et al., 2014; Lilja and Nilsson, 2015; Mandelstam, 2012)). Yet, various issues hamper the complete and accurate reconstruction of the human OR, particularly due to its characteristic high curvature (Fig. 1). A common observation is that the anterior extent of the Meyer’s loop is underestimated by most reconstruction methods currently employed in clinical research (Lilja et al., 2014). Indeed, an accurate Meyer’s loop tractography should produce a dense set of streamlines (Benjamin et al., 2014; Goga and Ture, 2015) with no separation or gaps between the fibres (Fig. 1, red circle), mirroring the known anatomy of the bundle (Ebeling and Reulen, 1988; Goga and Ture, 2015). A possible limitation comes from the inability of the diffusion tensor (DT) representation, which is often employed in clinical research, to resolve the underlying complex local directions of the WM fibre pathways (Tournier et al., 2011).

In addition, the impact of image acquisition on Meyer’s loop reconstruction remains unclear. Conventional whole-brain clinical dMRI acquisitions aim to reduce scan duration by limiting the number of diffusion encoding directions (e.g., between 12 and 60 at a single b-value) and spatial resolution (e.g., at best 2 × 2 × 2 mm^3 isotropic). From an acquisition point-of-view, imaging data with higher spatial resolution seems promising for capturing the intricacies and fine sharp turn of the Meyer’s loop. However, this often comes at a cost of reduced signal-to-noise ratio (SNR), which can be compensated for by increasing

![Image](https://example.com/image.png)

Fig. 1. Tractography of the optic radiation. Streamlines are colour coded by orientation (i.e., left-right: red, antero-posterior: green, superior-inferior: blue). Meyer’s loop is formed of streamlines sharply bending in the temporal lobe (left panel, dashed area). The red line (middle panel) shows the distance from Meyer’s loop to the temporal pole (ML-TP).
FSL EDDY (Andersson and Sotiropoulos, 2016) (fsl.fmrib.ox.ac.uk). Susceptibility distortions were also corrected using FSL TOPUP (Andersson et al., 2003) for both the Connectom and Prisma data. The Connectom data were additionally corrected for geometric distortions due to gradient non-linearity (Glasser et al., 2013). All data were then upsampled to $1 \times 1 \times 1 \text{mm}^3$ and aligned between scanners, using the Prisma standard data set as the reference frame for each subject.

This step facilitated the positioning of region-of-interests (ROIs), reducing subjective bias at the inter-individual level and allowed a direct comparison of tractography results between protocols. More specifically, the Connectom and Prisma data were affinely co-registered using the mean $b = 0$ and $b = 1200 \text{s/mm}^2$ images using ANTs (Avants et al., 2011), followed by appropriate B-matrix rotation (Leemans and Jones, 2009). Since the GE Excite-HD data were acquired without reverse phase encoding, images were non-linearly warped to the reference space to correct for susceptibility distortions.

2.3. Local modelling and tractography

Next, fibre orientation distribution functions (fODFs) were derived using multi-shell multi-tissue constrained spherical deconvolution (MSMT-CSD) (Jeurissen et al., 2014), for both Connectom and Prisma data. For the single b-value Std-40 mT/m data, free-water elimination was performed by only supplying the WM and cerebro-spinal fluid response functions to the MSMT-CSD algorithm in MRtrix. The resulting fODF peaks (thresholded at amplitudes $> 0.1$) were used to perform tractography using the FiberNavigator (Chamberland et al., 2014).

Tractography parameters were fixed for all subjects and protocols (angular threshold: 45°, step size: 1 mm, min/max length: 30/200 mm). For both hemispheres of each subject, a $5 \times 5 \times 5 \text{mm}^3$ seeding ROI was placed laterally to the LGN (Chamberland et al., 2017; Martinez Heras et al., 2015), with initial propagation direction oriented along the left/right axis (Fig. 2, purple). A negative ML-TP distance indicates a shorter ML-TP on the left side (e.g., larger anterior extent of the Meyer’s loop).

The ML-TP distance was measured using the axial projection of the most anterior part of the Meyer’s loop (i.e., the absolute Y-component of the 3D Euclidean distance). This distance was then normalized by head size using the most posterior point of each occipital pole (OP) (i.e., 100%($\text{ML-TP}$)/($\text{TP-OP}$)), allowing for inter-individual comparisons. Unless specified, all other instances of this measurement within this paper refer to the raw ML-TP distance. A one-way ANOVA was conducted to compare the effect of scanning protocol on the normalized ML-TP distance. Post-hoc results were corrected for multiple comparisons using the Bonferroni-Holm test. Finally, a lateralization index was derived for all sixty-five pairs of Meyer’s loop reconstructions by subtracting measurements of the right hemisphere from those of the left one. A negative value indicates a shorter ML-TP on the left side (e.g., larger anterior extent of the Meyer’s loop).

3. Results

The tract reconstructions were highly consistent with anatomical descriptions of the OR for all subjects. A representative reconstructed OR of a single subject across all protocols is illustrated in Fig. 3, using an oblique lateral view. In a direct side-by-side comparison, one can observe a larger anterior extent of the OR for the SoA protocols (e.g., blue and purple) when compared to data from the Std protocols. More importantly, even though the ML-TP distances are larger in the Std protocols, the tractography result from all data sets show dense reconstructions of streamlines in Meyer’s loop, with no separation between the streamlines. Coloured lines are drawn in the image space to better depict the intra-subject variance across protocols.

Fig. 4 illustrates the asymmetry of the Meyer’s loop reconstruction for 3 representative subjects, both qualitatively and quantitatively. In this figure, each row represents the same subject across different protocols. The axial planes were set so that the entire OR was visible (e.g., positioned below the deepest point of the Meyer’s loop in the Z axis).
Intra- and inter-subject variability of the anterior extent of the Meyer’s loop is revealed by the lateralization indices. A trend towards a left lateralization of the OR was found for both SoA protocols, although only significant for the 300 mT/m protocol. This is directly in line with other dissection and tractography studies that also observed a reduced ML-TP distance on the left hemisphere (de Gervai et al., 2014; James et al., 2015; Lilja et al., 2014; Mandelstam, 2012; Nowell et al., 2015; Yogarajah et al., 2009). In a recent study, a significant left lateralization of the OR was also found in a cohort of 90 children, but only in male subjects (Dayan et al., 2015). Another group also found a leftward lateralization of the OR using data from the Human Connectom Project, but only in terms of volume (Kammen et al., 2016).

4.2. Pre-processing and tractography choices

Potential sources of error can include registration, interpolation and the tractography algorithm itself. To begin with, our choice of registering the pre-processed data to a single reference space could potentially induce errors in distance measures, especially if the registration fails to properly align the volumes. However, visual inspection of
all datasets confirmed that good registration was achieved for all subjects. This was performed not only looking at the overlay of raw diffusion images, but also by inspecting the spatial organisation of the diffusion directions (i.e., fODF glyphs), with respect to the anatomy in all three planes. Moreover, performing the measurement comparisons in the native space of each acquisition might have introduced additional variance in the ML-TP distance, since the exact position of anatomical landmarks used for measurements cannot be guaranteed. In this work, we also chose to interpolate the diffusion data to the resolution of the anatomical data (i.e., 1 mm³) before modeling the fODFs. It has been shown recently that interpolating the raw diffusion volumes outperforms the direct interpolation of diffusion-derived measures (Dyrby et al., 2014).

Another point to consider following interpolation of the data is that data with different spatial resolutions have different partial volume effects. For most diffusion methods using a single b-value, it is a challenging task to correctly estimate the fODFs in the presence of cerebrospinal fluid (CSF), and our results derived from the Std-40 mT/m protocol may have been affected by this. Multi-shell modelling approaches can overcome these drawbacks at the tissue interfaces (Jeurissen et al., 2014). Additionally, the performance of multi-shell methods will typically increase with the total number of measurements acquired, leading to more accurate tractography (e.g., SoA datasets employed in this study). Finally, an inherent limitation to our study is that the true underlying fibre architecture of the Meyer’s loop is unknown for each subject, and thus the true ML-TP distance is also unknown.

4.3. Neurosurgical implications

From a clinical perspective, obtaining a physically-defined border of
a specific pathway (e.g., tip of Meyer's loop) is of main interest to minimize post-operative morbidity. Tractography is an invaluable tool for surgical planning, being the only tool available for neurosurgeons to visualize fibre pathways prior to surgery (Essayed et al., 2017; Nimsky et al., 2016) by super-imposing them onto surgical navigation scans. Multiple groups have attempted to model the OR using tractography for surgical planning (Borius et al., 2014; Chen et al., 2009; Lilja et al., 2015; Meesters et al., 2017; Nilsson et al., 2007; Novell et al., 2015; Yogarajah et al., 2009), suggesting a direct link between the ML-TP distance and VFDs (Chen et al., 2009). A more recent clinical study revealed that patients with VFDs had their Meyer's loop estimates located anterior to the resection margins, whereas in patients without VFDs, the Meyer's loop reconstruction did not reach as far as the resection area (Winston et al., 2012). Keeping these results in mind, one can consider a thought experiment in which a surgeon is about to perform ATLR on a patient whose data were acquired with the 40 mT/m protocol described here (e.g., Fig. 3, right). In that case, not knowing that the anterior aspect of the Meyer's loop depicted by this Std protocol is 7 to 12 mm behind what is inferred from more advanced acquisitions can be dramatic for the patient's outcome. This undershoot in ML-TP may in part explain why more than half of ATLR patients suffer from VFDs post-operatively (Chen et al., 2009; Winston et al., 2012; Yogarajah et al., 2009).

In light of these results, there remains little standardisation in the acquisition and reconstruction of diffusion data for surgical planning. Indeed, application of Meyer's loop tractography in neurosurgery greatly depends on detailed anatomical knowledge and on the effects of different acquisitions and analysis methods. OR reconstructions derived from tractography should be carefully interpreted since the possible post-surgical outcome for patients will be dependent on the hardware and protocol that is available in the hospital. A similar study to the current one but based on a large cohort of patients would therefore be valuable for the neurosurgical community.

4.4. Recommendations and future directions

Despite being unable to recover multiple fibre orientations, the diffusion tensor remains the most widely employed representation for surgical planning. Based on our Meyer's loop tractography results, being able to resolve complex fibre architecture seems crucial for every pipeline that aims to reconstruct the full anterior extent of the OR. Without the ability to accurately recover complex fibre configurations, tractography-recovered streamlines are prone to a premature halt in the WM.

In recent years, more advanced approaches have been proposed, surpassing the limitations of conventional DTI (Jeurissen et al., 2017; Tournier et al., 2011). MSMT-CSD is a promising new technique that provides sharper diffusion profiles, allowing the estimation of ODFs in complex regions. In addition, MSMT-CSD provides more precise WM fibre orientation estimates at the tissue interfaces, which is crucial for tracking to OR from the LGN. Although not focused on the Meyer's loop reconstruction, MSMT-CSD was also recently applied in a clinical study.
context to reconstruct the entire optic pathway of twenty-six paediatric tumor patients (Hales et al., 2018). Sixty diffusion gradients distributed over two shells (i.e., b = 1000 and 2200 s/mm$^2$) were used for a total scan duration of 7 min 50s, indicating that MSMT-CSD can be employed in a clinically feasible scan time.

Moreover, tractography methods are now at a stage where anatomical information can be introduced as input to help reduce false-positives and premature tract termination (for review, see (Jeurissen et al., 2017)). It is worth mentioning at this point that most of the aforementioned advanced tractography methods are already publicly available to clinicians via open-source software packages such as the FiberNavigator (chamber.github.io/fibernavigator_single), MRtrix (mrtix.org) and Dipy (nipy.org/dipy).

For those with limited access to SoA hardware and acquisition protocols, alternative strategies can be considered. From an acquisition point of view, it is suggested to balance between spatial and angular resolution (Sotiropoulos and Zalesky, 2017), with the latter having a better impact on tractography (Vos et al., 2016). From an image processing point of view, latest advances in image quality transfer (Alexander et al., 2014) may also be considered. Methodological advances in denoising and upsampling approaches (Dyrby et al., 2014) also help to improve both spatial and angular resolution. Furthermore, microstructure-informed tractography (Girard et al., 2017) is a novel addition to conventional tracking based on the idea that each fibre bundle possess unique microstructural features (e.g., axon diameter). These features can then be used to guide streamline propagation and potentially solve reconstruction ambiguities in regions of complex fibre architecture. In this work, we addressed this problem by incorporating prior anatomical information. Encoding such external prior information to the tracking is in great part responsible for achieving a complete reconstruction of Meyer's loop (Chamberland et al., 2017). Using the MAGNET algorithm, streamlines are allowed to undertake within-voxel sharp turns as they enter the directionally-encoded ROI (Fig. 2, green); a scenario that is not supported by most other tractography algorithms.

5. Conclusion

Taken together, we demonstrate that (where exactly the same tractography parameters are used) the choice of acquisition protocol affects Meyer's loop reconstruction. Specifically, acquiring data with a higher spatial and angular resolution (Vos et al., 2016) with more b-values gives rise to a more complete anterior delineation of the Meyer's loop, assuming that SoA reconstructions inferred from tractography do reflect Meyer's loop true location. This has important applications in ATLWR where surgeons may transect part of the Meyer's loop due to an under-estimation of its location. The results also underline, when time permits, the importance of using SoA imaging protocols for neurosurgical planning.

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Contributors

MC was responsible for conducting the study, data processing, statistical analysis and writing of the paper. CMWT was responsible for subject recruitment, data acquisition, data pre-processing and revising the manuscript. DKJ oversaw all aspects of the study and revised the manuscript.

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Ethics approval

The study was approved by Cardiff University - School of Psychology ethics committee and written informed consent was obtained.

Competing interests

None declared.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.nicl.2018.08.021.

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