A STEM-BASED DISSECTION OF INFERIOR FRONTO-OCCIPITAL FASCICULUS WITH A DEEP LEARNING MODEL

Pietro Astolfi[1,2,3], *Alessandro De Benedictis*[4], *Silvio Sarubbo*[5], *Giulia Bertó*[1,2], *Emanuele Olivetti*[1,2], *Diego Sona*[3], *Paolo Avesani*[1,2]

[1] NeuroInformatics Laboratory (NILab), Bruno Kessler Foundation, Trento, Italy
[2] Center for Mind and Brain Sciences (CIMeC), University of Trento, Italy
[3] PAVIS, Istituto Italiano di Tecnologia, Genova, Italy
[4] Neurosurgery Unit, Bambino Gesù Childrens Hospital, Roma, Italy
[5] Division of Neurosurgery, S. Chiara Hospital APSS, Trento, Italy

ABSTRACT

The aim of this work is to improve the virtual dissection of the Inferior Frontal Occipital Fasciculus (IFOF) by combining a recent insight on white matter anatomy from ex-vivo dissection and a data driven approach with a deep learning model.

Current methods of tract dissection are not robust with respect to false positives and are neglecting the neuroanatomical waypoints of a given tract, like the stem. In this work we design a deep learning model to segment the stem of IFOF and we show how the dissection of the tract can be improved.

The proposed method is validated on the Human Connectome Project dataset, where expert neuroanatomists segmented the IFOF on multiple subjects. In addition we compare the results to the most recent method in the literature for automatic tract dissection.

Index Terms— diffusion MRI, bundle segmentation, deep learning, IFOF, stem

1. INTRODUCTION

The aim of this work is to improve the virtual dissection of the Inferior Frontal Occipital Fasciculus (IFOF) [1, 2] by combining a recent insight on white matter anatomy from ex-vivo dissection and a data driven approach with a deep learning model [3]. A more accurate characterization of the IFOF might benefit pre-neurosurgery intervention planning and clinical studies on brain plasticity and brain disorders.

The anatomy of this neuroanatomical tract can be characterized in-vivo at the individual level from recordings of diffusion MRI [4]. After a first a step of diffusivity model reconstruction [5], and a subsequent step of fiber tracking [6] we may obtain a representation of structural brain connectivity, namely a tractogram, as a collection of millions of streamlines, where each streamline is encoded as a polyline. The task of tract dissection from a tractogram, referred also as virtual dissection in contrast to ex-vivo dissection, is concerned with the identification of those streamlines that have a specific neuroanatomical meaning. In this work we focus our contribution to the dissection of the IFOF.

The IFOF is an associative neuroanatomical tract and it connects parts of the occipital cortex, the temporo-basal area and the superior parietal lobule to different cortical regions in the frontal lobe. This formal definition can be encoded as logical expression with the white matter query language (WQML) [7] to select the streamlines that belong to the IFOF. The parcellation of Regions Of Interests (ROIs) with the termination points of streamlines can be obtained from an atlas after the normalization to a standard space. Even with an accurate ROI parcellation, the formal definition of IFOF is not enough to exclude many false positive streamlines, usually a by-product of sub-optimal tracking algorithms (see example in Fig. 1).

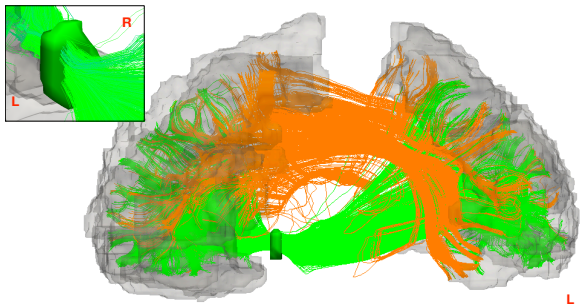

Fig. 1. Example of dissection of IFOF with stem-based segmentation (green) and the false positive streamlines (orange) not filtered out by considering only the regions of termination points. In the box the anatomy of stem.

Recent studies on ex-vivo microdissection (modified Klingler's technique) of the IFOF have provided a better characterization of the IFOF by detecting a peculiar waypoint [1, 2], called "stem" of IFOF (see box in Fig. 1). By definition, a stem is a region of the white matter where all the fibers of a fascicle are collected. The IFOF stem is located in the white matter of the ventral third of the external capsule, just medial to the putamen and ventral to the claustrum [1]. By including the stem as additional waypoint constraint to the WMQL rule definition, we may drastically reduce the number of false positive streamlines and reach a better in-vivo approximation of the true anatomy of the IFOF [2]. Unfortunately no brain atlas of white matter provides support to parcellate the stem of the IFOF.

In this work we present, StemSeg, a data driven approach that learns a supervised model for the segmentation of the IFOF stem and the subsequent virtual dissection of the IFOF. The task is cast as a segmentation problem of a volumetric image, and the output is a

We gratefully acknowledge the support of NVIDIA Corporation with the donation of the Titan Xp GPU used for this research.

three dimensional binary mask. Since a usual structural T1 MRI image does not provide enough information to discriminate the structure of the white matter, we refer to a coloured fractional anisotropy image (cFA), a derivative from the fitting of diffusion tensor model (DTI) on DWI recordings [4]. The cFA is capturing the information on local fiber orientation, and our working assumption is that the stem is characterized by streamlines with homogeneous fronto-occipital directions.

We trained a convolutional neural network (CNN) on a subset of the Human Connectome Project (HCP) dataset, and we tested the model on two sets of IFOF dissected with different strategies of manual dissection. We provide the empirical evidence that an automated stem-based IFOF dissection can be robust with respect to alternative strategies of manual dissection. In addition, we prove that our IFOF dissection outperform the state of the art method [8], which uses a deep learning model but is neglecting the anatomy of stem.

2. METHODS

2.1. Basic notation

We define a streamline as a sequence of l points $s = (x_1, \ldots, x_l)$, where $x_i \in \mathbb{R}^3$. A whole brain tractogram is defined as a set of streamlines, $T = \{s_1, .., s_N\}$, with $N \sim 10^5 - 10^6$. We denote a tract as a subset of streamlines from the tractogram, $t = \{s_1, .., s_n\}$ where $s_j \in T$ and $n \ll N$.

A whole brain volumetric image is denoted as $V_{i,j,k} = [i] \times [j] \times [k]$. An ROI is defined as binary mask by a function $\mathcal{V}_{ROI} : V_{i,j,k} \rightarrow \{0, 1\}$. A cFA image is defined as $\mathcal{V}_{cFA} : V_{i,j,k} \rightarrow \mathbb{C}^3$, where $\mathbb{C} = [0, 255]$ denotes the RGB encoding. A slice of a volume is defined as two dimensional plane, where $V_{i,j,\overline{k}}$, $V_{i,\overline{j},k}$ and $V_{\overline{i},j,k}$ are referring to axial, coronal and saggital projections respectively.

A dissection rule is defined as a logical expression of streamlines and ROIs, containing conjunctions and disjunctions of predicates. Referring to the WMQL syntax [7], we report here two predicates that we will use in our dissection rule: $endpoints\_in(s_i, V^{ROI})$ that is true when at least one of the termination points x_1^i and x_l^i of a streamline s_i is included in a binary mask V^{ROI}, and $waypoint\_in(s_i, V^{ROI})$ that is true when at least one point of the streamlines s_i is included in V^{ROI}.

2.2. CNN for stem segmentation

StemSeg is designed as a two steps method: a first step in charge of the segmentation of the stem, and a second step devoted to the dissection of the IFOF using the ROI of the stem, which we call stem-ROI, as additional clause of a dissection rule.

Even though the segmentation of the stem-ROI can be approached with a 3D CNN, such a model presents several computational issues due to 3D operations, which limit the network to learn only few local (small field of view) features. A common workaround is reformulating the task as several 2D image segmentations where CNN proved to be very effective, a strategy known as 2.5D segmentation. From the original volumetric representation $V_{i,j,k}$ we randomly sample 2D slices to train a 2D CNN considering the three different projections: $V_{i,j,\overline{k}}$ (axial), $V_{i,\overline{j},k}$ (coronal) and $V_{\overline{i},j,k}$ (saggital). The output of CNN is again a 2D slice containing a probability mask. The whole volumetric estimate of the stem is obtained by applying the trained CNN to all the slices of each projection sequentially, obtaining three values per voxel corresponding to the prediction for the three projections. The binary mask of the stem $\hat{V}^{stem}$ is summarized by merging the three values using a binarized average i.e., thresholding at 0.5.

```
IFOF.left = (
   endpoints_in(
      frontal_inferior_lobe.left
      OR frontal_middle_lobe.left
      OR frontal_superior_orbitalis.left)
   AND endpoints_in(
         occipital_lobe.left
         OR cuneus
         OR lingual
         OR parietal_superior
         OR precuneus)
   AND waypoints_in(stem.left))
frontal_inferior_lobe.left = (
   frontal_inferior_operculus
   OR frontal_inferior_orbitalis
   OR frontal_inferior_triangularis)
occipital_lobe.left = (
   occipital_superior
   occipital_middle
   occipital_inferior)
```

Table 1. WMQL formal dissection rule of left IFOF (black) extended with the stem (blue). The region names refer to AAL atlas.

The CNN model we used for learning the 2D slice segmentation is U-net [3], which is an encoder-decoder segmentation network. The encoder learns deep features by alternating convolutional layers with max pooling, which reduce the image resolution, while the decoder alternates convolutional layers with upsampling to reconstruct a prediction mask. Furthermore, the decoder concatenates at each layer features computed in the encoder at the same resolution, giving the network the U shape.

Which kind of MRI volume may enable an effective segmentation of the stem? DWI images are recordings information on fiber orientation. The fitting of a DTI model allows the estimation of the components of three main directions of diffusivity as a coloured fractional anisotropy (cFA) image: red for lateral, green for anteroposterior and blue for vertical. Since the stem of the IFOF is a waypoint where all the streamlines have a very homogenous fronto-occipital orientation, we may assume that such a region will be encoded by green colour in a cFA image. According to this assumption, we sampled our 2D slices from $V_{i,j,k}^{cFA}$ volumes.

2.3. Stem-based IFOF dissection

In the second step of StemSeg we dissect the IFOF using a WMQL [7] rule which extends the formal definition of the IFOF with the stem. A WMQL rule combine predicates and logical operators to define constraints for streamlines selection. Predicates usually test the condition whether a point of a given streamlines belongs to a ROI. According to recent neuroanatomy studies [1, 2], the termination points of streamlines of the IFOF should be located in several regions of occipital and frontal lobes. The detailed combination of these regions is reported in the formal WMQL rule of Table 1.

We refined the formal rule by imposing an additional constraint: at least one point of the streamlines of IFOF should belong to the ROI segmented as the stem of the tract. The conjunctive clause of $waypoint\_in$ is combined with the $endpoints\_in$ conditions (blue line in Table 1). The use of the stem as waypoint condition prevents the usual manual effort of defining exclusion regions to filter out false positive streamlines.

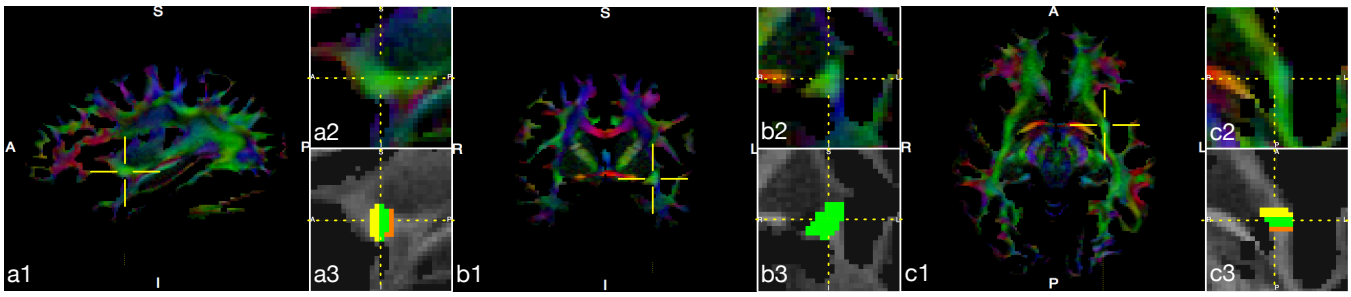

Fig. 2. An example of stem detection in the cFA. The three panels show the saggital, coronal and axial view of the center of mass of stem. Each small panel reports the detailed view of the stem region (upper) and the overlap between the labeled and predicted stem (lower): true positive (green), false negative (orange) and false positive (yellow).

3. EXPERIMENTS

3.1. Materials

We based our empirical analysis on the 3T HCP [9] dataset: 1.25mm DWI and the structural T1 images. We sampled such data from the last 158 acquired HCP subjects. We designed a pipeline to compute the diffusivity model both using DTI [10] and CSD [5], after extracting 90 gradients at b=2000. From the DTI we derived FA and cFA, while from the CSD combined with the deterministic local tracking algorithm [10] we generated the tractograms (uniform seeding in the voxels of white matter mask, step size 0.625mm).

Using all the 158 HCP subjects we built a dataset of labeled stem-ROIs used to train our CNN. The labelling of the stem-ROIs was supervised by a neuroanatomist, S.S., and followed the procedure used in [2]: (i) streamline filtering using the termination regions derived from [2] to the Automated Anatomical Labeling (AAL) atlas, (ii) manual definition of ROIs to exclude false positive streamlines, until a good IFOF dissection is achieved, (iii) manual segmentation of the stem-ROI in three consecutive coronal slices of the cFA. As result we obtained 316 stem-ROIs and 316 dissected IFOF, half of them in the right hemisphere and the other half in the left hemisphere. We call this collection of labeled data, **ROI-based** dataset.

ROI-based dissections even when performed by experts are not able to avoid all the false positive streamlines due to the coarse granularity of voxels. We considered to operate an additional IFOF dissection using a **bundle-based** procedure. A second expert neuroanatomist, A.D.B., dissected the IFOF on a subsample of 30 subjects using Tractome [11]. This tool supports a manual procedure of dissection based on interactive picking and removal of bundle of streamlines. We report the difference between the ground-truth (gt) IFOF dissected with a bundle-based and ROI-based strategy both qualitatively in Fig. 3a and 3b, and quantitatively by means of the volumetric DSC (see Section 3.2), obtaining $93.9 \pm 3.7\%$.

3.2. Experimental design

We designed an empirical analysis to assess how effective can be a method of IFOF dissection, like StemSeg, based on automated segmentation of the stem. We subsampled 128 subjects as training set of CNN, with a further split into 114/14 to perform model selection. The training was iterated for 500 epochs with learning rate 1e-3, using data augmentation and batches of 47 slices 2D, randomly sampled from different subjects. The cFA images were cropped from original size (145x174x145) to isotropic volumes (80x80x80), knowing that by definition the stem of the IFOF is located in the inferior, anterior, and lateral portion of an hemisphere of the brain. In the training procedure we optimized the binary cross-entropy (CE) loss, with weighting correction to better manage the class imbalance.

We tested the trained network over the remaining 30 subjects of the dataset, i.e., the subjects for which we have both ROI-based and bundle-based IFOF gt. We evaluated the stem-ROI prediction using two measures: the mean displacement of center of mass computed along the three axes, and the mean volumetric recall ($TP/TP + FN$). The first measure aims to assess whether the CNN has a direction bias in the segmentation, while the second measure is informative with respect to the dissection task, where a stem underestimation can lead to the loss of many IFOF streamlines.

The IFOF dissection of the 30 test subjects was performed by applying the rule in Table 1 with regions taken from AAL atlas [12], and co-registered to each subject through the non-linear ANTs SyN algorithm [13]. According to the best practice in literature we evaluated the result of dissection by computing the volumetric mask from the streamlines. Comparison between expert dissection and automated dissection was computed as overlapping the voxel masks by means of the volumetric Dice Similarity Coefficient (DSC) $DSC = 2TP/(2TP + FP + FN)$. A first comparison was carried out with respect to the IFOF dissected according to the ROI-based approach to test the accuracy of an automated stem-based method. A second comparison addressed the question of how robust is the proposed method with respect to a manual accurate procedure.

An additional experiment was designed to compare StemSeg with respect to TractSeg [8], the most prominent and recent method in the literature. TractSeg casts the dissection task as a problem of volume segmentation by encoding the streamlines representation of a tract in the corresponding voxel binary mask. The segmentation is performed by training a CNN following a 2.5D approach based on U-net in analogy to what we presented here. Differently from StemSeg, in TractSeg the CNN takes in input a simplified CSD model, where only the three main direction peaks are encoded in each voxel. We trained TractSeg adopting the default parameters reported in [8], using the same dataset split of the experiment above.

In both TractSeg and StemSeg we used the same code implementation available at https://doi.org/10.25663/brainlife.app.205. Furthermore, we published all the labelled stem-ROIs used to train StemSeg along with the learned parameters and the predicted stem-ROIs at https://doi.org/10.25663/brainlife.pub.8.

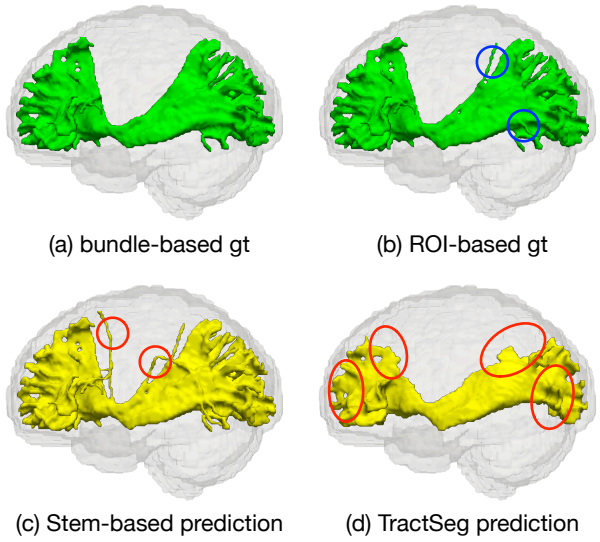

Fig. 3. Qualitative comparison of voxel masks of the two manual dissection procedures (green) and of the two automated dissection methods (yellow) for a left IFOF. The blue circles highlight the anatomical differences, while the red higlight prediction errors.

4. RESULTS AND DISCUSSION

For the stem-ROI segmentation we measured the mean displacement of the center of mass along the three axes: 0.33 mm (lateral), 0.82 mm (anteroposterior), 0.26 mm (vertical). The mean volumetric recall of the stem-ROI is 74.9±18.0. The results of the IFOF dissection with StemSeg and TractSeg on ROI-based and Bundle-based dataset are summarized in Table 2, and a qualitative example is reported in Fig. 3.

Method	ROI-based	Bundle-based
TractSeg	61.0 ± 5.6	62.1 ± 5.7
StemSeg	$\mathbf{98.8 \pm 1.0}$	$\mathbf{93.8 \pm 3.5}$

Table 2. mean DSC over 30 test subjects.

According to the empirical results reported in Table 2 we may claim that the automated segmentation of stem is a viable and effective method for IFOF dissection. A further analysis of the error in segmenting the stem-ROI reveals that the displacement of the center of mass, with respect to the correct location, is negligible both in vertical and lateral directions (see Fig. 2b3). While the displacement error in the anteroposterior direction is higher (see Fig. 2a3 and 2c3), and it is responsible for the high variance in the recall score, it does not impact the accuracy of IFOF dissection. This distribution of the displacement error reflects the variance of manual labelling of stem-ROIs.

As mentioned in the introduction, ROI-based dissection tends to have more false positive streamlines while bundle-based dissection allows the pruning of all outlier streamlines (see Fig. 3b and 3a respectively). StemSeg is performing well (see Table 2), even with respect to a manual and time demanding dissection.

StemSeg clearly outperforms TractSeg as reported in Table 2. The large gap between the DSC measures is mainly motivated by the two different data representations: streamlines for StemSeg and voxels for TractSeg. Fig. 3c and 3d, show an example of the IFOF anatomy dissected by StemSeg and TractSeg respectively. Despite using the same examples of StemSeg, TractSeg is missing the portion of superior regions, both frontal and occipital, where streamlines are fanning out. This pattern can not be properly detected with a voxel-based representation.

5. REFERENCES

[1] S. Sarubbo et al., "Frontal terminations for the inferior fronto-occipital fascicle: anatomical dissection, DTI study and functional considerations on a multi-component bundle," *Brain Structure and Function*, vol. 218, no. 1, pp. 21–37, Dec. 2013.

[2] J. Hau et al., "Cortical Terminations of the Inferior Fronto-Occipital and Uncinate Fasciculi: Anatomical Stem-Based Virtual Dissection," *Frontiers in Neuroanatomy*, vol. 10, May 2016.

[3] O. Ronneberger et al., "U-Net: Convolutional Networks for Biomedical Image Segmentation," in *MICCAI 2015*. 2015, pp. 234–241, Springer International Publishing.

[4] P. J. Basser et al., "MR diffusion tensor spectroscopy and imaging.," *Biophysical journal*, vol. 66, no. 1, pp. 259–267, Jan. 1994.

[5] J. Tournier et al., "Robust determination of the fibre orientation distribution in diffusion MRI: Non-negativity constrained super-resolved spherical deconvolution," *NeuroImage*, vol. 35, no. 4, pp. 1459–1472, May 2007.

[6] P. J. Basser et al., "In vivo fiber tractography using DT-MRI data," *Magnetic resonance in medicine*, vol. 44, no. 4, pp. 625–632, 2000.

[7] D. Wassermann et al., "The white matter query language: a novel approach for describing human white matter anatomy.," *Brain structure & function*, vol. 221, pp. 4705–4721, Jan. 2016.

[8] J. Wasserthal et al., "TractSeg - Fast and accurate white matter tract segmentation.," *NeuroImage*, vol. 183, pp. 239–253, Aug. 2018.

[9] D. C. Van Essen et al., "The WU-Minn Human Connectome Project: An overview," *NeuroImage*, vol. 80, pp. 62–79, Oct. 2013.

[10] E. Garyfallidis et al., "Dipy, a library for the analysis of diffusion MRI data," *Frontiers in Neuroinformatics*, vol. 8, no. 8, pp. 1+, Feb. 2014.

[11] D. Porro-Muñoz et al., "Tractome: a visual data mining tool for brain connectivity analysis," *Data Mining and Knowledge Discovery*, vol. 29, no. 5, pp. 1258–1279, 2015.

[12] R. S. Desikan et al., "An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest," *NeuroImage*, vol. 31, no. 3, pp. 968–980, 2006.

[13] B. B. Avants et al., "Symmetric diffeomorphic image registration with cross-correlation: evaluating automated labeling of elderly and neurodegenerative brain," *Medical image analysis*, vol. 12, no. 1, pp. 26–41, 2008.