AUTOMATIC DELINEATION OF WHITE MATTER FASCICLES BY LOCALIZATION BASED UPON ANATOMICAL SPATIAL RELATIONSHIPS.

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ABSTRACT

Delineation of white matter fascicles is generally achieved with tractography by specifying seeding and exclusion regions of interest (ROIs) defined by anatomical landmarks. In practice, the most popular approach has been to manually draw the ROIs for each scan which requires extensive training, is strongly subject to inter- and intra-expert variability and is highly time consuming. Fully automatic localization of the ROIs is of central interest, particularly for white matter investigations involving a large number of subjects. In this work, we propose an original approach in which the ROIs are localized using the fuzzy set theory by discovering *stable anatomical spatial relationships* in the brain anatomy. Our approach relies on a learning procedure, in which stable relationships are identified from a limited number of training templates supplied with manually delineated ROIs. For a new subject, the spatial relationships are applied and the ROIs localized. We show that our approach enables successful automatic delineation of the ROIs in the individual. Importantly, we show that this localization is robust across subjects age.

Index Terms— DWI, Tractography, Region of Interest, Fuzzy spatial relationships

1. INTRODUCTION

Measuring the water diffusion with magnetic resonance diffusion weighted imaging (MR-DWI) has enabled non-invasive investigation of the white matter (WM) in the brain. In a number of applications, DWI is paired with tractography in order to localize and characterize WM fascicles of interest. For example, fascicles such as the motor pathways (corticospinal tract), the optic radiations, the language pathways or the corpus callosum can be successfully localized. Tractography recovers the fascicle pathway by delineating highly anisotropic trajectories of diffusion passing through selection ROIs and originating in seeding ROIs. These ROIs are generally manually drawn by an expert for each subject based on the anatomical knowledge of known fascicle trajectories. Exclusion ROIs can also be employed to exclude those tract streamlines that pass through regions that are not anatomically plausible.

The most widely used approach requires manually drawing seeding, selection and exclusion ROIs prior to tractography. This, however, is highly time consuming, requires extensive training and is strongly subject to inter- and intra-expert variability. Automatic fascicles delineation has raised increasing interest in the literature. A number of approaches have focused on performing whole brain tractography and subsequently clustering the fascicles using a known atlas of fascicles [1]. Other approaches have focused on automatically delineating the seeding, selection and exclusion ROIs prior to tractography, such as by elastically aligning a manually delineated atlas of ROIs [2]. Recently, [3] proposed to estimate the consensus ROIs with STAPLE [4] after non-rigid alignment of a collection of templates with manually delineated ROIs.

A natural alternative for the localization of neuroanatomical regions such as tractography ROIs is to describe them with spatial relationships which are stable across subjects. Spatial relationships are ubiquitous in natural language descriptions found in neuroanatomy textbooks and are naturally utilized by experts when manually drawing ROIs for tractography. For example, the lateral geniculate nucleus, which is a primary relay center along the optic tracts, is typically described as a "*small structure that protrudes slightly from the posteroinferior aspects of the thalamus*" [5]. Spatial relationships have, however, scarcely been employed in *automatic* brain image analysis. To our knowledge, only a few MR segmentation approaches have investigated the use of spatial relationships by integrating them either in a deformable model [6] or in a Markovian segmentation framework [7].

In this work, we propose for the first time to automatically delineate ROIs based upon a description with *fuzzy anatomical spatial relationships* with respect to known anatomical landmarks in the brain. Our approach relies on a learning procedure to discover stable spatial relationships from a limited number of templates with manually delineated ROIs. For analysis in an individual target subject, these relationships rules are represented by 3-dimensional fuzzy maps in the *fuzzy set theory* framework and combined together using information fusion between fuzzy sets [8]. We show that our SPAtial RELation ROI (SPAREL-ROI) approach enables

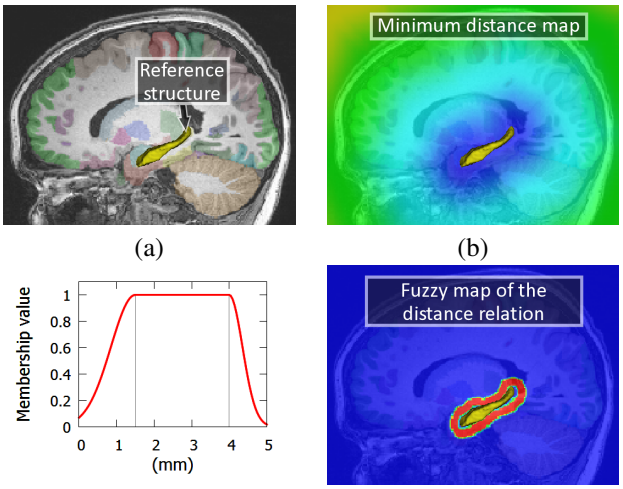

Fig. 1. The fuzzy map for a distance relation is constructed in two steps. First the image of the minimum distance of each voxel to the reference structure (a) is computed (b) (blue=close; green=far). Second, a fuzzification function (c) is applied, whose parameters describe the imprecise distance of the target object with respect to the reference. This leads to the fuzzy map (d) describing the distance relationship (blue=0; red=1).

successful delineation of the ROIs in the individual. We compared SPAREL-ROI to the multiple template fusion approach described in [3] and show that our approach can provide superior localization and is more robust to age disparity between the templates and the target subject.

2. MATERIAL

Fuzzy spatial relationships. The imprecise nature of spatial relationships is known to be well modeled by *fuzzy set theory* and the possibilistic framework [8]. Importantly, this provides us with flexible tools for information fusion across fuzzy sets which can be used to combine multiple spatial relationships. Following the approaches of [8, 6, 7], we represent spatial relationships as 3-dimensional *fuzzy* maps in a possibilistic framework. Here, we currently consider only distance relationships that describe the distance of a target object with respect to a reference object (Fig. 1).

Automatic learning of the spatial relationships in the anatomy. We consider a set of T templates $(\mathcal{T}_1, \ldots, \mathcal{T}_T)$, each of them being supplied with a T1-weighted image $\mathcal{T}_t^{\mathrm{T1W}}$, a manual delineation of the ROIs $\mathcal{T}_t^{\mathrm{manualROI}}$, a diffusion tensor image $\mathcal{T}_t^{\mathrm{DTI}}$ and an image of anatomical landmarks $\mathcal{T}_t^{\mathrm{landmarks}}$ utilized as reference objects when learning the spatial relationships. The images share the same coordinate system defined by $\mathcal{T}_t^{\mathrm{T1W}}$. In this work, the anatomical landmarks $\mathcal{T}_t^{\mathrm{landmarks}}$ were provided by an automatic parcellation of $\mathcal{T}_t^{\mathrm{T1W}}$ in multiple cortical and subcortical structures.

For each ROI r, we estimate the mean and standard deviation of the minimum distance $(\mu_{r,l}^{\min}, \sigma_{r,l}^{\min})$ and maximum distance $(\mu_{r,l}^{\max}, \sigma_{r,l}^{\max})$ between the ROI and each anatomical landmark $l \in \mathcal{T}_t^{\mathrm{landmarks}}$ among the templates. In the following, we consider only the L distance relationships with smallest $\sigma_{r,l}^{\min} + \sigma_{r,l}^{\max}$ which amounts to considering only the L most stable spatial relationships in the anatomy. Additionaly, we identify the major fascicle orientation in each ROI r. To this end, we consider the fascicle orientations to follow a 3-dimensional Gaussian distribution $\mathcal{G}(\mu_r^{\vec{v}}, \sigma_r^{\vec{v}})$ whose parameters are estimated based upon the manually drawn ROIs and the principal eigen vector $\vec{v_i}$ of each tensor in the templates $\mathcal{T}_t^{\mathrm{DTI}}$. Our complete learning procedure is synthesized by the following *pseudo-code*:

```
FOR each ROI r to learn
  FOR each landmark l in T_t^landmarks
    Determine (μ_{r,l}^min, σ_{r,l}^min, μ_{r,l}^max, σ_{r,l}^max) among templates
  ENDFOR
  Determine (μ_r^v, σ_r^v) from T_•^DTI
ENDFOR
```

Delineation of the ROIs in a target subject. We consider a subject $\mathcal{S}$ in which the ROIs will be automatically delineated. For each ROI r, the 3-D fuzzy maps of the L most stable distance relationships identified in the learning procedure are computed (see Fig.1d). The maps are combined together using the conjunctive fusion operator between fuzzy sets described in [8] in order to form a fuzzy localization map of the ROI r in $\mathcal{S}$ (see Fig.2c).

The localization is refined by using the knowledge of the expected fascicle orientation in the ROI. We consider the tensor image $\mathcal{S}^{\mathrm{DTI}}$ and compute at each voxel i the membership $m_i \in [0,1]$ of the fascicle orientation $\vec{v_i}$ to the estimated Gaussian fascicle orientation distribution $\mathcal{G}(\mu_r^{\vec{v}}, \sigma_r^{\vec{v}})$ by $m_i = \exp(-\frac{(\vec{v_i}-\mu_r^{\vec{v}})^2}{2(\sigma_r^{\vec{v}})^2})$. m_i verifies $m_i = 1$ when the orientation at voxel i exactly matches the estimated mean orientation $\mu_r^{\vec{v}}$ in the training ROIs. The fascicle orientation membership map and the fuzzy localization map are combined by conjunctive fusion. Finally, the membership values are thresholded, leading to the automatic delineation of the ROI r. The localization procedure is synthesized by the following *pseudo-code*:

```
FOR each ROI r to localize in S
  FOR the L landmarks l with smallest (σ_{r,l}^min + σ_{r,l}^max)
    F_{r,l} ← Fuzzy map of the distance relationship
              with respect to l
              using (μ_{r,l}^min, σ_{r,l}^min, μ_{r,l}^max, σ_{r,l}^max).
  ENDFOR
  F_r ← Fusion of the L fuzzy maps (F_{r,1}, ..., F_{r,L})
  F_r ← Fusion of F_r with G(μ_r^v, σ_r^v) from S^DTI
  Final ROI ← Threshold F_r
ENDFOR
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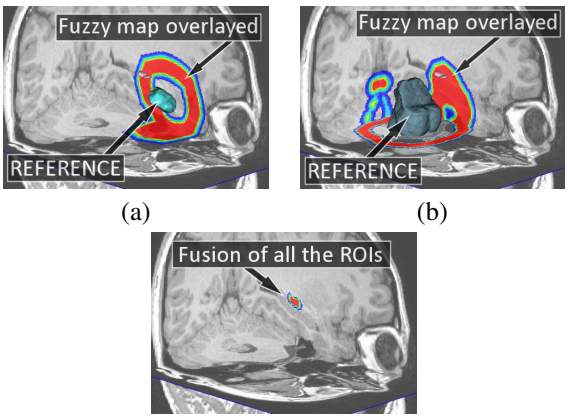


Fig. 2. Illustration of two automatically extracted stable spatial relationships to describe the left LGN. Relationship with respect to the amygdala (a); relationship with respect to the brain stem (b); and the final fusion of the L stable relationships describing the left LGN (c).

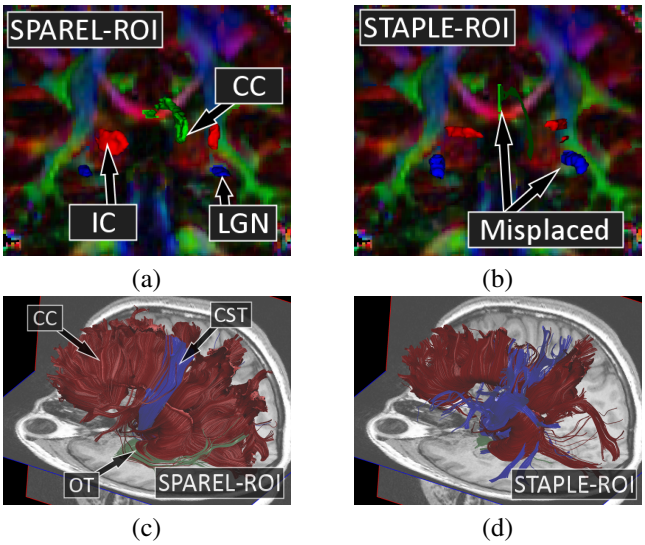


Fig. 3. Localization of the ROIs in an individual by SPAREL-ROI (a) and STAPLE-ROI (b). With STAPLE-ROI the regions in the CC and in the LGN are misplaced, probably due to errors in the elastic registration. Resulting tractography when seeding from SPAREL-ROI (c) and STAPLE-ROI (d). It shows SPAREL-ROI to provide much better results.

3. METHODS

Our training dataset $(\mathcal{T}_1, \ldots, \mathcal{T}_T)$ was composed of $T = 9$ healthy controls (age: 16-25yo; mean age: 19.8yo; standard deviation: 2.9yo) with good quality T1-weighted (T1w) MPRAGE and DWI acquisitions. Our approach requires the definition of anatomical landmarks necessary to compute the spatial relationships. In this work, we consider a parcellation of the T1w

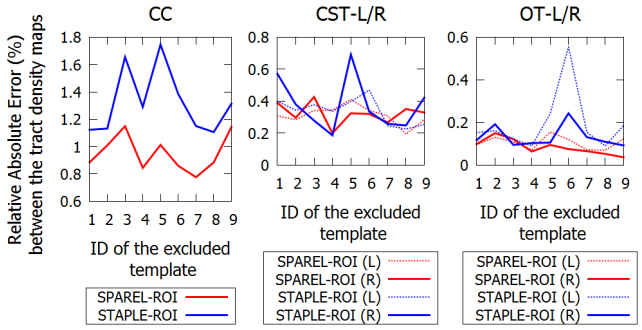
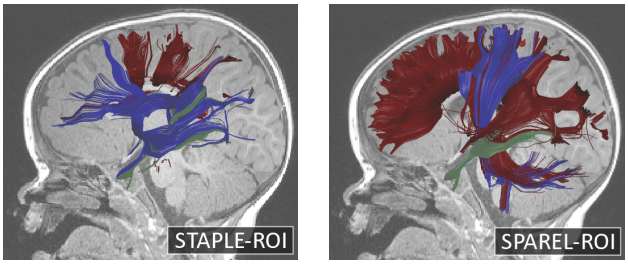


Fig. 4. Assessment of the ROI delineation performance. We achieved $T = 9$ different ROIs delineations by excluding each time a different template. For each excluded template $\mathcal{T}_t$, we automatically delineated the ROIs of $\mathcal{T}_t$ with SPAREL-ROI and STAPLE-ROI and achieved tractography. For each structure (CC, CST L/R, OT L/R), we computed a fascicle density image, quantifying both the spatial extent and the density of the localized fascicles. The fascicle density images obtained when using the automatically and manually (ground truth) ROIs were compared by assessing the Root Mean Squared Error (RMSE).

image in 114 cortical and subcortical structures based on a multiple-template fusion approach [4] utilizing 18 templates provided by the Center for Morphometric Analysis at Massachusetts General Hospital (IBSR). The DW-images were aligned with affine registration to the T1w image. We currently considered the delineation of five WM fascicles: the corpus callosum (CC), the left and right corticospinal tracts (CST L/R) and the left and right optic tracts (OT L/R). To illustrate our approach, we currently adopted a seeding strategy for the delineation of the fascicles which is based on one seeding ROI per fascicle. These five ROIs were manually delineated in each template by expert inspection of color-FA images. The manual delineation protocol is described as follows. CC: one sagittal slice in the body of the corpus callosum; CST L/R : five axial slices in the L/R internal capsule (IC); OT L/R : six coronal slices in the L/R lateral geniculate nucleus. We compared our SPAREL-ROI approach to the approach proposed by [3] referred to as STAPLE-ROI.

First, we qualitatively compared both the delineated ROIs and corresponding tractography[1] when using SPAREL-ROI and STAPLE-ROI for a subject not included in the training dataset. Second, we performed a leave-one-out experiment and quantitatively compared the SPAREL-ROI and STAPLE-ROI. Finally, we compared SPAREL-ROI and STAPLE-ROI on a one-year-old subject which is a very different age compared to the age of the subjects in our training dataset.

[1] In this work, all tractography experiments were achieved with the same parameters: FA stopping criterion:0.15; angle stopping criterion: 40 degrees; 15 tracts per voxel of the ROI



(a) (b)

Fig. 5. Automatic ROI delineation and tractography with a 1 y.o. subject with STAPLE-ROI (a) and SPAREL-ROI (b).

4. RESULTS

We first report the results of the ROIs' delineation for a single subject. Fig.3a-b illustrates the estimated ROIs for IC, CC and LGN and Fig.3c-d the final tractography outcome. Fig.4 illustrates the results from the leave-one-out validation, demonstrating that our SPAREL-ROI approach results in superior delineation of the fascicles of interest than those generated using the STAPLE-ROI method. It also shows SPAREL-ROI to be more stable to the choice of the training dataset. Finally, Fig.5 illustrates that SPAREL-ROI provides more anatomically accurate results when applied to a subject whose age was very different compared to the age of the subjects used in the training dataset.

5. DISCUSSION

We proposed a fully automatic approach for the delineation of WM fascicles based on the description of the brain anatomy with fuzzy spatial relationships. We have demonstrated that our SPAREL-ROI approach outperforms STAPLE fusion of the ROI templates (Fig. 4) and is more robust age disparity between the templates and the target subject (Fig. 5).

Importantly, our approach requires the definition of anatomical landmarks to compute the spatial relationships. Here we considered a brain parcellation computed with a template-fusion approach. We remark that such a multi-template parcellation may be perturbed the same way the multi-template ROIs (STAPLE-ROI) [3] is. However, our results (Fig.3, Fig.4 and Fig.5) indicate that small errors in the registration of the *parcellation templates*, which invariably propagate error to the localization of the landmarks, has far less impact than registration error in the *ROI templates* (Fig.3a-b). In SPAREL-ROI, the landmarks are only used as a proxy to incorporate the imprecise knowledge of the brain anatomy provided by spatial relationships. Ultimately, the fusion of the fuzzy spatial relationship maps provides better results by being more robust to registration errors and to template-to-individual age differences (Fig.5). In this work we currently considered only distance relationships across anatomical objects (Fig.1,2). We demonstrate that fusion of such distance relationships enables accurate localization of the ROIs and accurate delineation of the fascicles. Particularly, we showed that the fusion of distance relationships can successfully describe a single-slice ROI such as the ROI in the body of the CC. In contrast, the fusion of misaligned single-slice ROI templates in STAPLE-ROI can lead to a poor agreement between the templates and to a poor localization of the fascicles (Fig. 5).

In future work we will assess the benefits of describing the brain anatomy with additional spatial relationships such as orientation and symmetry relationships and will investigate the performance of SPAREL-ROI with pathologic brains. We additionally expect to expand our collection of template ROIs for the automatic delineation of more complete collections of major WM fascicles of the brain in individuals.

6. REFERENCES

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