

# Radial Diffusivity template of Corpus Callosum. Correlation with normal aging.

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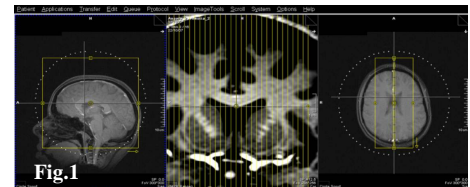
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**Introduction.** Most MRI studies investigating white matter (WM) changes in relation to the normal aging process detected changes in the water diffusion related MRI indices [1,2]. These changes mainly occur in frontal WM, both lobar and corpus callosum (CC). In particular the radial diffusivity (DR) index, but not the axial diffusivity (DA) one, was able to differentiate the genu of CC of elder people compared to younger ones [3,4]. DR describes the diffusion properties of water molecules in the direction perpendicular to the fiber bundles and is recognized, by recent studies, to be strictly related to the myelin membranes status [5,6]. The recently developed GIOTTO technique [7] allows for the extraction of high-resolution and precise DR maps of the CC. Thanks to high resolution these volumes are suitable for good quality non-linear co-registration between the CC of more subjects. Thus we integrated the GIOTTO DR measurement with a semi-automated non-linear registration procedure (the non-linear step was based on the b-spline algorithm by Rueckert et al. [8]). We extracted a mid-sagittal CC DR template on 35 healthy subjects spanning 6 decades (between 20 and 80 years). We used the DR template to individuate the CC region in which the normal aging process significantly correlates with the DR changes, thus suggesting age related myelination changes in fiber bundles crossing the CC.

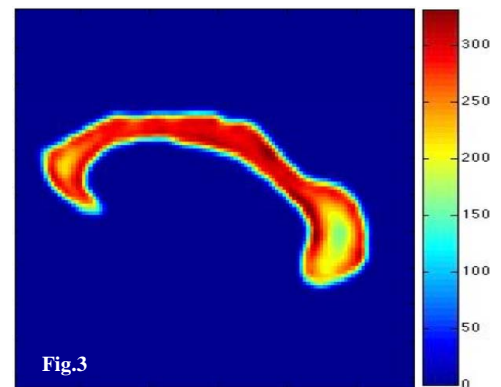
**Methods.** All MRI was performed on an Allegra Siemens 3T scanner. GIOTTO technique was applied to 35 healthy subjects aging 20 to 80 years (40±18). 29 sagittal slices were acquired, with the central one positioned on the mid-sagittal section of CC (see Fig.1). GIOTTO acquisition included 32 diffusion weighted volumes and 8 diffusion un-weighted volumes (b0). After DR maps extraction, the central slice of each subject was used to create the mid-sagittal CC DR template. Registration steps are summarised in Fig.2. A pixel by pixel correlation between age and DR was performed (p-value of 0.001 was set to define significance). All post-processing was implemented by home-made MATLAB scripts (The Mathworks, Inc., Natick, Massachusetts).

**Results.** The DR template is shown in Fig.3. Correlation results are shown in Fig.4a,b,c. Two ROIs (depicted as I and II in Fig.3b) are clearly identified by correlation analysis, one in the genu and one in the posterior portion of central body. Both regions showed an average increase of DR across the six decades of about the 25%.

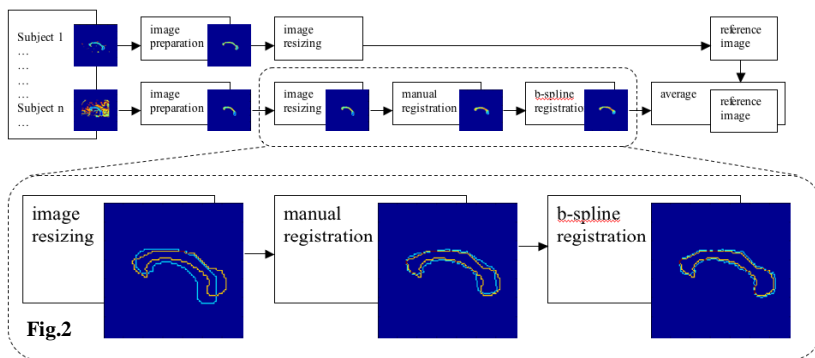
**Discussion.** The results in the genu of CC fit with previous MRI findings and with the well-known age related decline of mental processes superintended by the prefrontal cortex, an area strongly connected to the anterior part of CC. It is not trivial to speculate on the correlation found in the posterior part of the body. The highlighted region is probably connected with the sensory-motor cortex, as suggested by inspection of the results of Park et al. [9] in a parcellation guided segmentation of CC.



**Figure 1.** MPRAGE was used as localizer in the coronal projection to position of the 29 slices in order to cut the CC on its mid-sagittal section. The slice thickness was 2.7 mm.

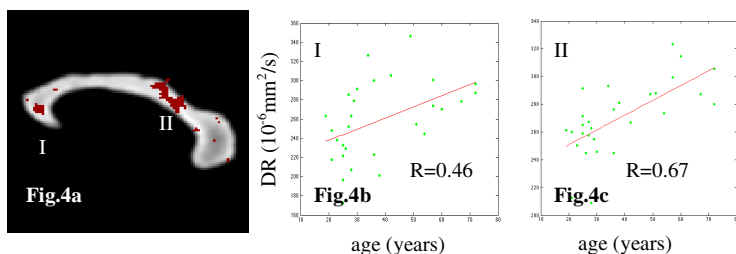


**Fig.3**



**Fig.2**

**Figure 2.** For each subject in the preparation step the mid-sagittal section of CC was manually segmented, guided by the b0 images, and by a DR threshold value set to  $600 \times 10^{-6} \text{ mm}^2/\text{s}$ . A manual registration step (resizing, shearing and rotating) and a b-spline registration step followed, in which the second subject CC was registered to the first subject one, the third subject CC was registered to the mean of the first and second subject ones and so on. The MATLAB scripts by Dirk-Jan Kroon (University of Twente, “Region growing” function and “Non-rigid b-spline grid image registration” tool) and by Valerio Luccio (NYU Center for Brain Imaging, <http://cbi.nyu.edu/software/>, “dinipti” function and “NifTImatlab” tool) were integrated in our MATLAB processing software.



**Fig.4a**

**Fig.4b**

**Fig.4c**

**Figure 3.** The mid-sagittal CC DR template. Color-bar scale is in  $10^{-6} \text{ mm}^2/\text{s}$ . The red colour indicates higher DR values suggesting the presence of less myelinated axons and/or thinner myelin sheets. The lowest values of DR (more myelin content) are found in the splenium and secondarily in the genu of CC.

**Figure 4.** a) pixel by pixel correlation analysis result (red pixels = significant correlation). b) correlation analysis of the 35 <DR> values obtained averaging all pixel values in ROI I. c) correlation analysis of the 35 <DR> values obtained averaging all pixel values in ROI II.

## References

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