In Vivo Measurement of Axonal Diameter and Density of Human Corpus Callosum Using Bi-Gaussian Model Q-planar MRI

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Introduction

The corpus callosum (CC) is the main fiber tract connecting bilateral cerebral hemispheres, serving information transfer and processing in various cognitive functions. Different CC regions might be affected differently in the development of disease, and their structural parameters such as size and shape might associate with cognitive or functional tests involved in different modes of interhemispheric interactions. Previously we proposed a novel magnetic resonance imaging method called q-planar imaging (QPI), which could in vivo map the relative axonal diameters and density of CC in human brain [1]. We also used k-means cluster analysis to segment the CC based on the QPI parameters, displacement and probability, to further visualize the difference in the computed axonal diameter and density distribution for each voxel [2].

It is known that water signal decay in a MR diffusion experiment in neuronal tissues, at sufficiently high diffusion weighting, appears to be non-mono-exponential, thus complicating even further the interpretation and assignment of the different components to actual physiological compartments [3, 4]. Therefore, we used 2D bi-Gaussian model (i.e. slow and fast components) to fit our QPI data. After 2D Fourier transformation of the slow and fast Gaussian curved surfaces of signal decay, respectively, two Gaussian curved surfaces of displacement distribution (i.e. narrow and broad components) were obtained. Intracellular and extracellular information could then be extracted from the narrow and broad Gaussian displacement distributions, respectively. Our results demonstrated that bi-Gaussian fitting QPI produced reasonable distribution of relative axonal diameters of CC in normal human brain.

Materials and Methods

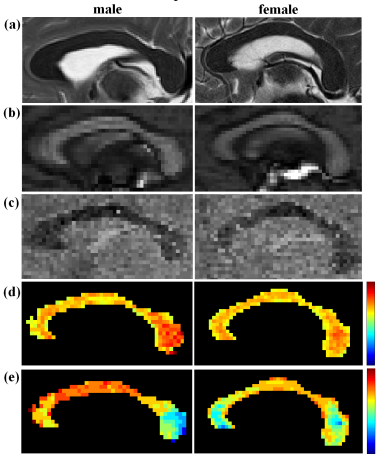
The CC images in the mid-sagittal plane were acquired from 12 healthy subjects (age: 22-32, M/F: 8/4, all right handedness) using 3T MRI system (Tim Trio, Siemens MAGNETOM, Germany). A multi-slice fast spin echo sequence was performed to obtain T2-weighted (T2W) images with in-plane resolution = 0.55 mm, and slice thickness = 2.5 mm. Images of QPI were acquired using a spin echo diffusion-weighted echo planar imaging (EPI), TR/TE = 1000/142 ms, in-plane resolution = 1.7 mm, slice thickness = 10 mm. The diffusion-weighted images were obtained corresponding to 1009 diffusion-encoding directions on a mid-sagittal plane. These encodings directions comprised of isotropic 2D grid points within a round circle of the radius of 18 increments corresponding to b values changing incrementally from 0 to 5000 s/mm^2. The total scan time for QPI was about 17 minutes.

For QPI data analysis, the 2D signal decay of the diffusion data in the q-plane was first fitted with a 2D bi-Gaussian function, and the two Gaussian curved surfaces of signal decay were then obtained (i.e. slow and fast components). According to Fourier relationship between the signal intensity and the displacement probability in q-space, 2D Fourier transform of signal attenuation in the q-plane was the projected displacement distribution of water molecules inside the tissue [5]. We performed 2D Fourier transformation of the slow and fast Gaussian curved surfaces of signal decay with respect to the q values which produced two Gaussian curved surfaces of displacement distribution (i.e. narrow and broad components). From the full area at half height of narrow (slow) Gaussian curved surfaces of displacement distribution, relative axonal diameters of callosal fibers (displacement mapping) can be acquired. The probability at zero displacement was given by the height of the distribution at zero displacement of narrow (slow) component, which provided information about relative axonal density. After obtaining the indices of displacement and probability of each CC, the individual values of each index were normalized to their own means for group comparison. In contrast, other two parameters extracted from the broad (fast) Gaussian curved surfaces of displacement distribution provided information about extracellular space and density.

Results and Discussions

Fig. 1d shows the mapping of the probability of water molecular at zero displacement of narrow (slow) component. Fig. 1e shows the mapping of narrow (slow) displacements in CC. The mapping of these two metrics provides spatial distribution of the relative axonal diameter in CC, inaccessible to T2W images, anisotropy or mean square length mapping (Fig. 1a, b, c). In the region-based analysis, the mean probability calculated from the splenium (CC5) was significantly larger than those from other regions ($p < 0.01$) (Fig. 2a). The mean displacement calculated from the splenium was significantly smaller than those from other regions ($p < 0.01$) (Fig. 2b). These results indicate that the relative axonal diameter of the callosal fibers in the splenium is the smallest and densest. Our results are consistent with Aboitiz's results [6] (Fig. 2c, d). In variance with Wiltelson's results showing gender difference at CC1 and CC4, no significant difference was found in this study [7]. The negative result may arise from the small number of subjects.

There are several advantages of the proposed QPI. The relative displacement in each pixel is used to provide novel image contrast indicating relative axonal diameters. Structural information beyond the spatial resolution of conventional MRI can be inferred without resorting to a complicated tissue model. Lastly, the scan time of 17 min makes clinical study highly feasible.



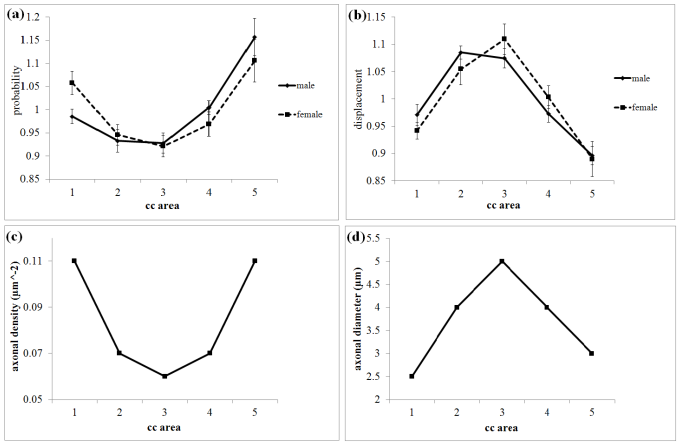


Fig. 1 Sagittal CC mappings of (a) T2WI, (b) anisotropy, (c) mean square length (d) probability, and (e) displacement in representative male (left column) and female (right column) normal subjects.

Fig. 2 (a) Probability and (b) displacement distribution of CC in male and female subjects. (c) Mean axonal density and (d) mean axonal diameter of human CC found by histology.

Conclusions

We have proposed a QPI method with bi-Gaussian fitting to map the distribution of relative axonal diameters and density in human CC. Our results are consistent with the previous reports. Being a diffusion MRI-based methodology, our results demonstrate the feasibility of QPI on clinical scanners, and show the potential for morphometric mapping of callosal fibers in disease brains.

References

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