

Simple global measures describing the complexity of the white matter architecture can provide useful information when analyzing diffusion MRI data, and can be even capable of finding statistical differences between groups. We propose the use of the fractal dimension of the FA maps for that purpose, and illustrate its potential on a dataset composed of elderly subjects and patients from three different stages of Alzheimer's disease.

Purpose and Motivation

- The fractal nature of diffusion MRI images has been studied before^{1,2}. However, to the best of our knowledge, fractal descriptors have not been employed as markers of disease.

- Simple fractal measures, such as the fractal dimension as estimated with the box counting technique, can provide a simple yet useful procedure to obtain information about the complexity of the white matter architecture.

Methods

- Four groups of subjects from an Alzheimer study were analyzed:
 - A:** Healthy control group (N = 17, 74 ± 3.5y).
 - B:** Patients with mild cognitive impairment (N = 13, 76.3 ± 1.1y).
 - C:** Patients with mild Alzheimer's disease (N = 19, 76.1 ± 2.7y).
 - D:** Patients with moderate Alzheimer's disease (N = 7, 76.6 ± 1.4y).
 Diagnosis according to NINCDS-ADRDA Alzheimer's Criteria.

- After preprocessing and diffusion tensor estimation, Fractional Anisotropy (FA), Mean Diffusivity (MD) and Radial Diffusivity (RD) maps were computed. The FA maps were afterwards slightly eroded in order to remove possible outliers. From them, binary maps can be obtained simply by thresholding the FA maps.

- The Hausdorff fractal dimension can describe how much a certain pattern changes when the scale at which it is measured also changes. For the calculation of fractal properties, the box counting method, which approximates the Hausdorff fractal dimension, is commonly employed. Using this method, the (3D) space is partitioned in equal boxes of size r . Then, $N(r)$ is the number of boxes of size r that contain at least a non-zero voxel. The estimation of the fractal dimension, FD, is performed by computing the slope of $N(r)$, when plotted in a double logarithmic scale.

- The notion of fractal dimension can also be extended to gray-level images. In this case, $N(r)$ is the mean value inside each box, instead of the number of non-zero voxels.

- FD values for the binarized FA maps (using a threshold of FA=0.3) and for the gray-level FA maps were computed for all subjects, together with mean values over the white matter of the FA, MD and RD maps. A one-way Anova test was performed to investigate whether the four groups belong to the same distribution. When they did not, bilateral t-tests were applied to check for pairwise differences.

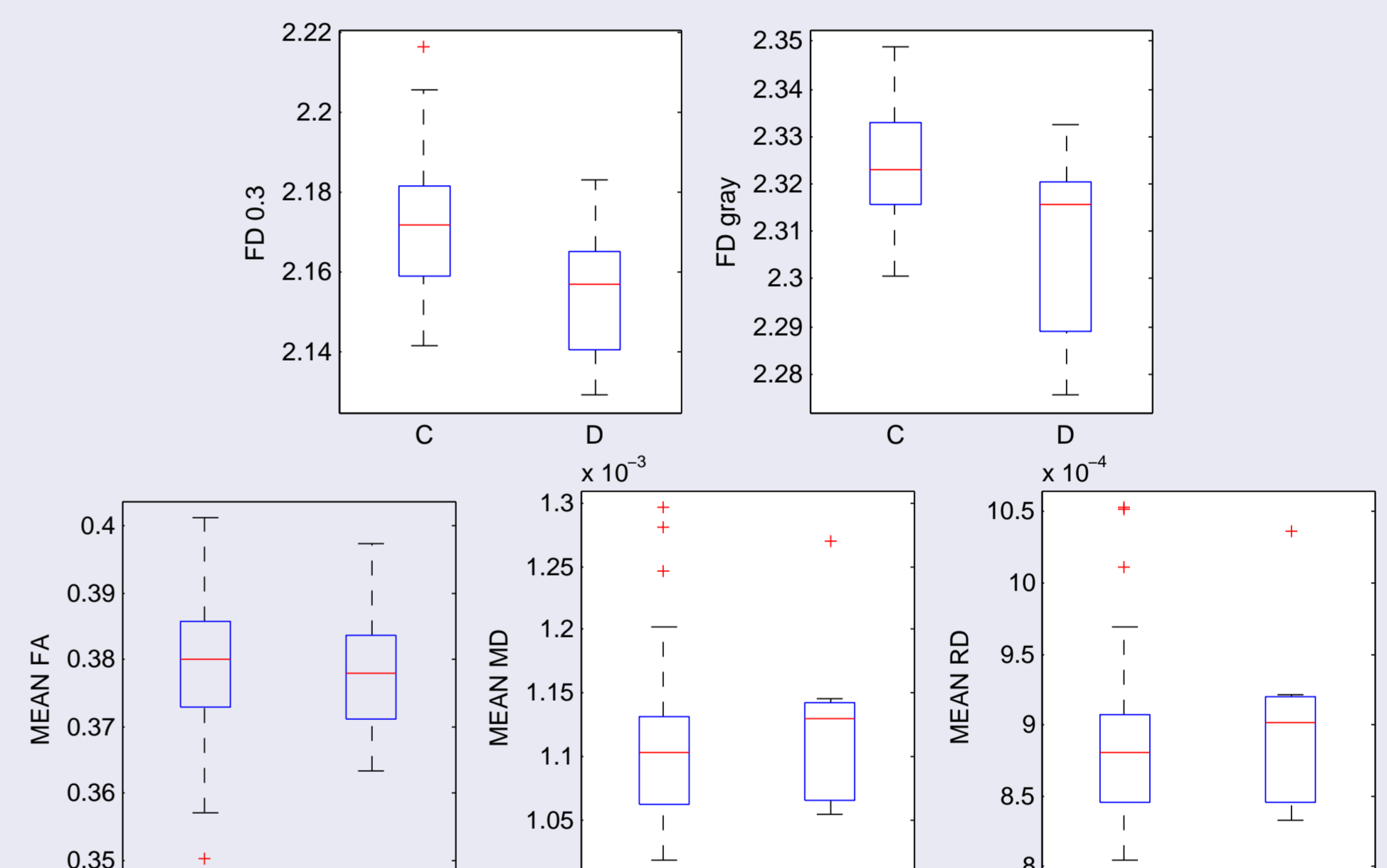
Diffusion weighted images were acquired in a GE Signa 1.5 T MRI unit at QDiagnóstica, Valladolid, Spain. The parameters of the acquisition protocol were the following: 25 gradient directions, one baseline volume, $b = 1000$ s/mm², 1.015 x 1.015 x 3 mm³ of voxel size, TR = 13,000 ms, TE = 85.5 ms, 256 x 256 matrix, NEX = 2 and 39 slices covering the entire brain.

Results

- Table below collects the p-values corresponding to the Anova and t-tests carried out. Significant differences were found for the FD over the binarized (FD 0.3) and gray-level FA (FA gray) maps, while no significant differences were found using the mean FA values. There is extensive literature indicating that MD and RD are more powerful descriptors of the changes within the white matter in Alzheimer's disease and, accordingly, significant differences were also found for the mean values of these maps.

- With regard to the pairwise comparisons, the FD 0.3 (and, to a lesser extent, the FD gray) showed a considerable capacity to differentiate subjects at different stages of Alzheimer's disease. Notably, both FD measures found significant differences between groups C and D, while mean MD and mean RD discovered significant differences between groups B and C.

MEASURE	ANOVA	A-B	A-C	A-D	B-C	B-D	C-D
FD 0.3	<10 ⁻³	0.027	0.005	<10 ⁻³	0.93	0.04	0.023
FD gray	0.0012	0.076	0.054	<10 ⁻³	0.86	0.039	0.009
MEAN FA	0.29	-	-	-	-	-	-
MEAN MD	<10 ⁻³	0.15	<10 ⁻³	<10 ⁻³	0.046	0.038	0.63
MEAN RD	<10 ⁻³	0.15	<10 ⁻³	<10 ⁻³	0.055	0.044	0.62



Conclusions

- Fractal dimension of FA maps is a simple yet useful method for providing global descriptors of the white matter architecture.
- In a group study on Alzheimer's disease, FD was able to reveal significant differences between subjects at different stages of the disease.

References

- [1] P. Katsaloulis, P. Verganelakis, A. Provata, Fractal dimension and lacunarity of tractography images of the human brain, *Fractals* 17(02): 181-189, 2009.
- [2] P. Katsaloulis, A. Ghosh, et al, Fractality in the neuron axonal topography of the human brain based on 3-D diffusion MRI, *The European Physical Journal B* 85: 150, 2012.

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