DTI IN THE CLINIC: EVALUATING THE EFFECTS OF SMOOTHING

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INTRODUCTION

The accuracy and interpretation of results obtained by Diffusion Tensor Imaging (DTI) are largely influenced by several experimental parameter settings. In Voxel-Based (VB) analysis images are smoothed, in order to improve their Signal to Noise Ratio (SNR) and to reduce the impact of normalization and artifacts. This is a critical step and care must be taken so that directional information and boundary structures are preserved throughout the smoothing process. Although, Gaussian smoothing is generally applied as a preprocessing step in VB analysis, the choice of kernel dimension seems to strongly affect values and locations of the detected white matter abnormalities (1). Moreover, probably because of the intrinsic anisotropic nature of the diffusion Gaussian filtering is likely to induce consistent partial volume effects.

An alternative approach (2) is to perform isotropic smoothing in homogeneous regions and anisotropic smoothing near boundary regions, thus enhancing the SNR of images, but preserving white matter boundaries. This smoothing technique involves an iterative process with a non–homogenous diffusion equation, and is performed individually for each diffusion–weighting direction, after optimisation based on the complete set of diffusion weighted images (2).

Aim of the present study was to compare results obtained by anisotropic smoothing and conventional Gaussian smoothing. The two smoothing approaches were evaluated for their capability to separate differential effects between patients and controls in a standard VB analysis, in order to assess the best approach for a clinical setting, with its specific requirements regarding efficient calculation, accuracy, sensitivity and specificity for pathologic alterations.

METHODS

Thirty subjects (mean±SD age 71.2±9.3 years) with Alzheimer Disease (AD) and thirty age- and sex-matched healthy subjects were recruited for this study. All examinations were performed on a 3.0 T MR scanner (Siemens Magnetom Allegra). DTI images were collected using a 2D SE EPI sequence (TR/TE=6700/77 ms; resolution=1.5 x 1.5 x 3 mm^3; 40 contiguous slices; NEX=4; 12 non-coplanar directions with b=1000 s/mm^2 and one image with b=0 s/mm^2). Three such DTI series were acquired for each subject.

DTI datasets underwent brain extraction and coregistration. For each subject, the tensor was calculated with a regularization approach that avoids negative eigenvalues, FA maps were derived from the tensor and averaged across series. The averaged FA maps were taken as a reference. FA maps with variable degree and quality of smoothing were created using data from a single series only. For Gaussian smoothing the Kernel Dimension (KD) has been varied from 3 mm to 16 mm; for anisotropic smoothing the Number of Iterations (NI) has been varied from 1 to 10. All FA maps were normalized to a study specific template.

A standard quantitative patient/control analysis was performed. Statistical significance was tested voxel-by-voxel by means of a two-tailed two-samples T-test (SPM5). Difference in FA was deemed as statistically significant if P<0.001 (uncorrected), and if the cluster size exceeded 19 voxels. The same statistical analysis was performed for the unsmoothed dataset, and the relevant results were used as reference. Effects of smoothing were evaluated by computing, for each level of smoothing, the False Positive Rate (FPR), defined as FP/N, and the accuracy, defined as (TP+TN)/(P+N).

RESULTS

Significant AD related reductions in FA were observed for all degrees and quality of smoothing. For the Gaussian dataset, the FPR had a minimum (0.009) for KD=3 mm and increased monotonically as a function of KD (Figure 1). For anisotropic dataset, the percentage of FP voxels initially decreased as a function of NI showing a minimum (0.006) at NI=4 and then mildly increased (Figure 1). For Gaussian smoothing the accuracy decreased monotonically (r>0.99, P<0.0001) as a function of KD, from 0.9970 to 0.9837 (corresponding to more than 1000 voxels False Positives); for the anisotropic approach the accuracy was rather independent (r<0.2, P>0.6) from NI at 0.9969±0.0004, (mean±SD).

DISCUSSION

Our findings showed that, for Gaussian filter, the FPR largely increased as a function of KD. Moreover, in agreement with (3), this result demonstrated that the approach of analyzing data with gradually increasing the KD until maximum sensitivity is found (1) could lead to significant artifactual effects (FPR). For anisotropic smoothing, the FPR was more stable across different smoothing parameters than the Gaussian smoothing. This outcome suggests that anisotropic smoothing is more appropriate than Gaussian smoothing in DTI applications, not only in optimal conditions (NI= 4; KD = 3 mm, for this study), but even under suboptimal conditions. In fact, although the accuracy was comparable for the two smoothing techniques this parameter was rather constant across the NI, while it rapidly decreased, with increasing KD. In conclusion, our results confirmed that the choice and amount of smoothing is crucial in clinical DTI studies because it can influence the results obtained in a VB analysis attesting differences between patients and controls. Although anisotropic smoothing seemed to be preferable in this respect, a moderate level of smoothing is preferred, considering the artifacts introduced by this manipulation.

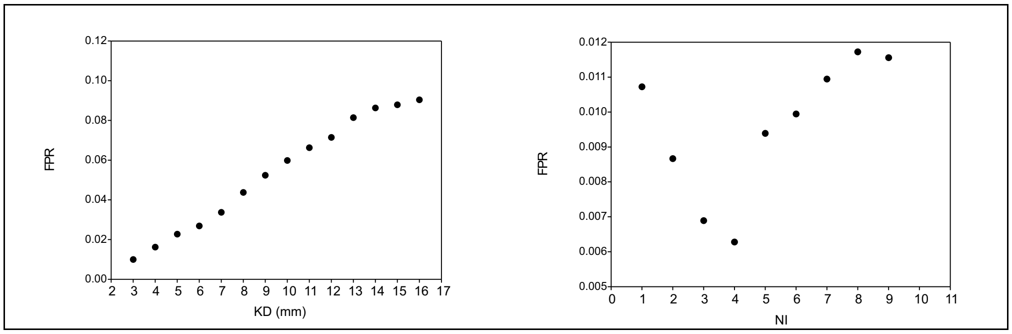

Fig1. The FPR as a function of the KD for Gaussian smoothing (left) and the NI for anisotropic smoothing (right).

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