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# Patch-Based Morphometry: Application to Alzheimer's Disease

Pierrick Coupé<sup>1,2</sup>, José V. Manjón<sup>3</sup>, Vladimir Fonov<sup>2</sup>, Simon F. Eskildsen<sup>2</sup>, D. Louis Collins<sup>2</sup> and The Alzheimer's Disease Neuroimaging Initiative \*

<sup>1</sup> Laboratoire Bordelais de Recherche en Informatique, Unité Mixte de Recherche CNRS (UMR 5800), 351 cours de la Libération F-33405 Talence cedex

<sup>2</sup> McConnell Brain Imaging Centre, Montreal Neurological Institute, McGill University, Montreal, Canada. University, 3801 University Street, Montreal, Canada H3A 2B4

<sup>3</sup> Instituto de Aplicaciones de las Tecnologías de la Información y de las Comunicaciones Avanzadas (ITACA), Universidad Politécnica de Valencia, Camino de Vera s/n, 46022 Valencia, Spain

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## Learning objectives:

1. To develop a new Patch-Based Morphometry method in order to enable more accurate anatomical comparison between populations.
2. To evaluate the proposed method on AD population compared to normal controls.

**Topic area:** Early detection and tracking

**Keywords:** Voxel-based morphometry, biomarkers, magnetic resonance imaging, hippocampus, temporal lobe, para-hippocampal cortex.

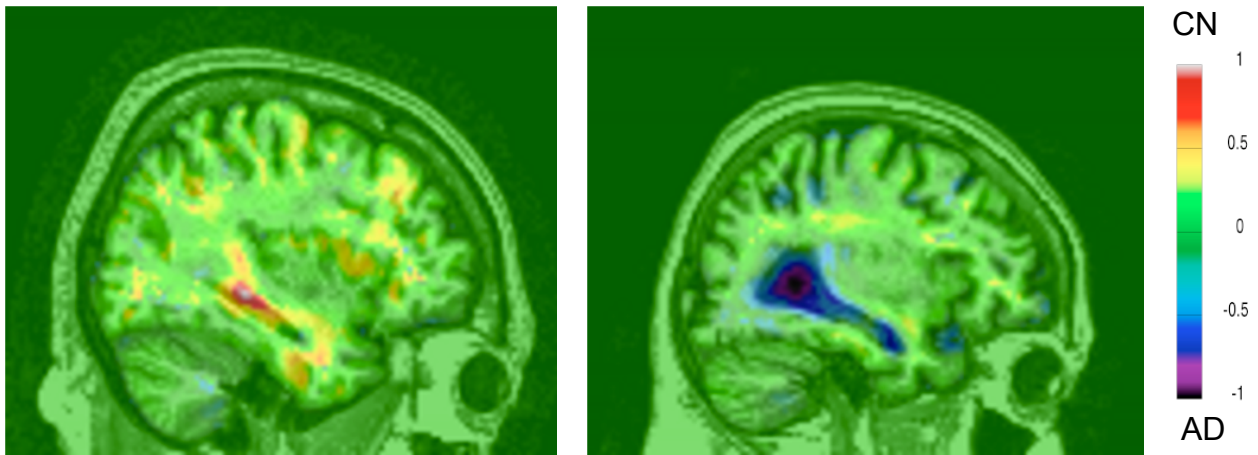
**Background:** While widely used to detect morphological differences between groups, Voxel-Based Morphometry (VBM) [1] is based on the assumption of one-to-one anatomical mapping between subjects and Gaussian distributions of focal tissue densities during statistical testing. To make data fit this model, tissue densities are blurred with large kernels at the expense of focal accuracy. To these issues, we propose a new Patch-Based Morphometry (PBM) method derived from our recently proposed innovative method to detect fine anatomical changes in MRI called *Scoring by Nonlocal Image Patch Estimator* [2]. SNIPE takes advantage of non-local analysis to handle the one-to-many mapping between brain anatomies. In this study, we extend SNIPE to the whole brain before comparing populations with PBM scores.

**Methods:** We randomly selected 50 MRI from cognitive normal (CN) subjects and 50 MRI from AD patients from the ADNI database. Step 1: the 100 images were processed as described in [2] (inhomogeneity correction, intensity normalization and rigid registration to MNI-ICBM152-nonlinear). Through a leave-one-out procedure, SNIPE was applied on each of the MRI scans using 30 images from each population as training templates. Step 2: all grading maps were nonlinearly registered to the MNI-ICBM152-nonlinear template with ANIMAL [3]. Step 3: a non-parametric Kruskal-Wallis test was performed at each voxel to estimate statistical differences between populations.

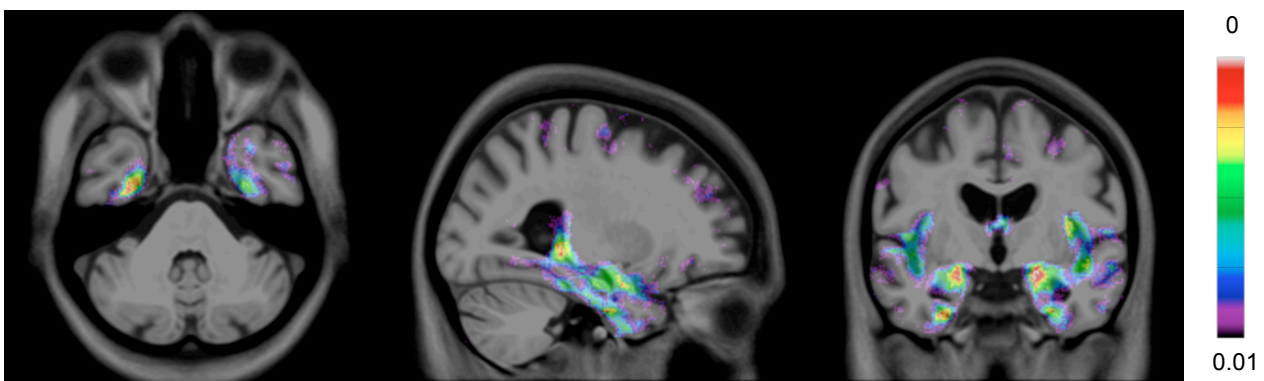
**Results:** Examples of grading maps are presented in Figure 1. Figure 2 shows the  $p$ -values overlaid on the MNI-template. Maximum differences between AD and CN were found in hippocampus and para-hippocampal areas, entorhinal cortex and in the temporal lobe around the lateral sulci and insula. Moreover, diffuse differences appear within the

gray matter. These results are consistent with previous VBM results [4]. We also noted an important difference around the superior mammillary notches as previously reported in volumetric studies [5].

**Conclusion:** In this proof of concept study, we showed that PBM produces results consistent with previously published VBM studies. However, contrary to VBM, these results were obtained without a blurring step since PBM can work at the voxel resolution. Further work will investigate optimal parameters for SNIPE and the possibility of using multivariate tests.



**Figure 1:** *Left:* SNIPE map for a normal control aged of 77 years with an average grading value of 0.7. *Right:* SNIPE map for a patient with AD aged of 78 years with an average grading value of -0.5. Values close to 1 (red) indicate areas where the image is more similar to CN population and value close to -1 (purple) indicate areas where the image is more similar to AD population. The maps are displayed in the MNI space after rigid registration (Step 1).



**Figure 2:** Patch-based morphometry (PBM)  $p$ -values (colour map thresholded to 0.01) derived from individual SNIPE maps (step 1), non-linearly registered (step 2) and overlaid on the MNI template (step 3) showing maximum differences between AD and CN in hippocampus, para-hippocampal areas, entorhinal cortex, insula and and in some lateral sulci.

## References

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