# Comparison of two VBM arithmetic based on Alzheimer's Disease MRI analysis

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**Abstract— Objective In order to study the difference of process and result, both optimized VBM and DARTEL arithmetic were used in the MR images of Alzheimer's Disease . Materials and Methods Baseline and 3 years longitudinal MCI controls were enrolled in the study. Gray matter differences of the whole brain were assessed using both method. Results. Both method has grey matter atrophy in bilateral superior temporal gyrus, parahippocampa gyrus, right anterior cingulate,right cerebellum anterior lobe. But the clusters of the optimized VBM is smaller than the DARTEL. Further more, some anatomic region can't be reported in the optimized VBM.Conclusion DARTEL is more robust than the optimized VBM based on AD MRI analysis.**

***Key words- DARTEL; Alzheimer's Disease; optimized VBM; MRI***

## I. INTRODUCTION

As the most common form of dementia, Alzheimer's disease (AD) currently affects more than 60 millions peoples in China. The patients may have some pathological damage, such as neuritic plaques, neurofibrillary tangles and synapse loss of cortical neurons[1]. With the development of aging society in our country, AD patients will give a heavy burden to the families and society. In recent years, scientific interest has also focused on mild cognitive impairment (MCI), a pre-dementia stage increased risk of future diagnosis of dementia, relative to the general population[2]. MCI is considered as a transitional stage between normal aging and dementia. So the early diagnosis and the treatment will be necessary to control the convertion from MCI to AD.

Voxel-Based Morphometry (VBM) [3]method was used to evaluate the gray matter (GM) and white matter (WM) morphological changes of the living brain based on the structure MR images. This method could objectively detect the differences in local brain regions and the brain tissue composition. In this study, we compare the differences between optimized VBM method and VBM-DARTEL(Diffeomorphic Anatomical Registration Through Exponentiated Lie) method. In addition, based on the same longitudinal MCI groups' scans, we used two different VBM methods respectively and carried out a longitudinal analysis. This study explore the probable results with different algorithms.

## II. MATERIALS AND METHODS

### *A. Image acquisition*

The Alzheimer's Disease Neuroimaging Initiative (ADNI) builded in 2003 is a consortium study to observe NC, MCI, and AD[4]. All data were all got from ADNI's MRI examinations of the brain were performed on a 3.0 T MRI scanner. We acquired a high-resolution T1-weighted MagnetisationPrepared Rapidly Acquired Gradient echo (MP-RAGE) 3D-sequence. Including TR/TE=8600ms/3.8ms, FOV=240mm*220mm, a pixel matrix=240mm*220mm, matrix size= 256×224, TI=900 ms, flip angle=9.

TABLE 1：Demographic variables and CDR for the different groups.

| Group | Baseline | 3-year |
|---|---|---|
| Sample size (male/female) | 12/5 | 12/5 |
| Age(years±SD) | 72.8±10 | 75.9±10 |
| CDR(0.5/1/2) | 19/0/0 | 7/6/4 |

The baseline was the group which did MRI scans for the first time. The 3-year was the same group which did MRI scans after 3 years.The CDR was a numeric scale used to quantify the severity of symptoms of dementia. It characterized six domains of cognitive and functional performance: memory, orientation, judgment & problem solving,

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community affairs, home & hobbies, and personal care [5]. CDR score was useful to vary the level of impairment: 0 = No impairment, 0.5, 1, 2, and 3 indicated very mild, mild, moderate and severe dementia. Details are shown in table 1。

*B. Image processing*

The ways of two method were processed in SPM8 (www.fil.ion.ucl.ac.uk/spm/, London, UK) .

- VBM and optimized VBM method

Wright[6] presents an initial conception of structural brain MR image analysis based on voxel in 1995. Ashburner and Friston[7] formally presented Voxel-Based Morphometry in 2000.From then on,VBM method attracts more and more researchers' eyes in recent years. VBM is a morphometry based on voxel. It is a whole-brain,unbiased technique for characterizing regional cerebral volume and tissue concentration differences in structural magnetic resonance images.

The data processing of VBM is showed in Fig 1.

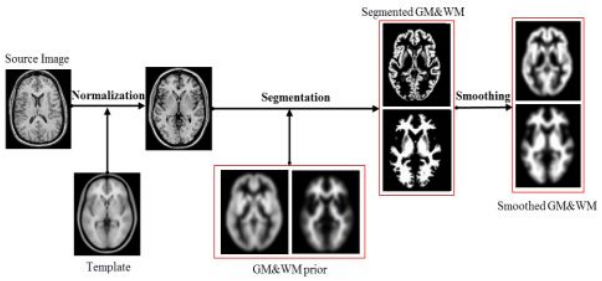


Figure 1 Procedure of VBM method

Spatical normalization based on the MRI template, involves transforming all the subjects' data to the same stereotactic space.and then doing affine trasform from original image to template image,and then correcting in part of non-linear deforrmation.the purpose of spatical normalization is correcting the difference of whole brain.After normalization, scans were segmented into gray matter (GM) , white matter(WM) and cerebrospinal fluid(CSF) based on prior probability of brain and the information of gray-scale image. Next, the image after segmented were smoothed with the full-width at half maximum (FWHM) of Gaussian smoothing kernel.The general kernel of gaussian function is

$$g(x)=\frac{\exp(-\frac{x^2}{2s^2})}{\sqrt{2\pi s^2}} \qquad (s=\frac{FWHM}{\sqrt{8\ln(2)}})$$

At last, statistical analysis is using voxel-based morphometry from GM or WM,then we can get the significative result.

However, the conventional VBM protocol have changed the intensity of image during the spatical normalization. Thereafter,the segment arithmetic is based on image intensity and prior probability of brain. Inspection of segmented images from the simple pre-processing procedure described above often showed several small areas of missegmented nongrey matter. Good et.put forward the optimized VBM arithmetic in 2001[8].

Optimized VBM arithmetic put forward segmentation shall be based on the native space. In order to preserve the volume of a particular tissue (GM or WM) within a voxel, a further processing step is incorporated. This involves modulating voxel values in the segmented images by the Jacobian determinants derived from the spatial normalization step. The Jacobian determinants is

$$J=\begin{bmatrix} j_{11} & j_{12} & j_{13} \\ j_{21} & j_{22} & j_{23} \\ j_{31} & j_{32} & j_{33} \end{bmatrix}=\begin{bmatrix} \partial x'/\partial x & \partial x'/\partial y & \partial x'/\partial z \\ \partial y'/\partial x & \partial y'/\partial y & \partial y'/\partial z \\ \partial z'/\partial x & \partial z'/\partial y & \partial z'/\partial z \end{bmatrix}$$

In this equation, $(x,y,z)$ and $(x',y',z')$ is the pixel of image before registration and after registration.During the modulation of image,we can get the volume of tissue by multiplying the value of pixel and Jacobian determinants.By this way,VBM arithmetic can analyse both density and volume.

The detailed step of optimized VBM has been done as following. (1)Normalization,set the normalizaed scans with the voxel size of 1mm*1mm*1mm, perserve amount the images with the standard T1 template. (2)Segmenation,all scans would be segemented into GM,WM and CSF. (3)Smooth, the C1 images applied a 8-mm full-width at half maximum (FWHM) Gaussian kernel for the statistical analysis(C1 is GM image after segmenation).

- DARTEL method

Dartel (Ashburner, 2007)[9] is a framework that was intended to achieve more accurate alignment among the brains of different subjects.

The DARTEL is parameterized by a single flow field, which is considered to be constant in time. With this model, the differential equation describing the evolution of a deformation is

$$\frac{d\Phi(x)}{dt}=u(\Phi^{(t)}(x))$$

$u$ is a flow field to be estimated.Generating a deformation involves starting with an identity transform $\Phi^{(0)}(x)=x$ and integrating over unit time to obtain $\Phi^{(1)}(x)$.

$$\Phi^{(1)}(x)=\int_{t=o}^{1}u(\Phi^{(t)}(x))dt$$

The Euler method is a simple integration approach, which involves computing new solutions after many successive small time-steps $(n)$.

$$\Phi^{(t+h)} = \Phi^{(t)} + hu(\Phi^{(t)})$$

This steps is equivalent to

$$\Phi^{(t+h)} = (x + hu) \circ \Phi^{(t)}$$

Different time step $h$ can got different deformation field $\Phi$.

Simultaneously minimize the sum of likelihood component from the sum of squares difference

$$(\sum_i (g(x^i) - f(\Phi^{(1)}(x_i)))^2)^{1/2}$$

And the $\Phi^{(1)}(x)$ parameterized by $u$.

In group theory, the flow field may be considered as a member of the Lie algebra , which is exponentiated to produce a deformation, which is a member of a Lie group . A useful result is that the Jacobian of a deformation that conforms to an exponentiated flow field is always positive. This ensures the mapping is diffeomorphic.

The image processing steps of DARTEL include AC-PC correction, segmentation, spatial normalization modulation, Affine transformation to Montreal Neurological Institute (MNI) space, Smoothing, Analysis. The specific process is shown ind figure 2.

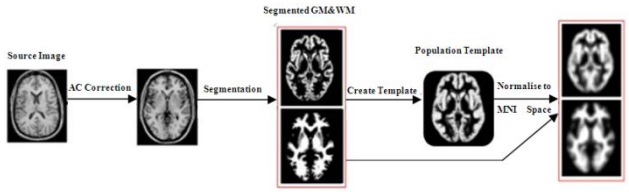


Figure 2 Procedure of DARTEL method

Creating template is the most important step in DARTEL.This step takes the average of all images as the initial template, and got the final template by iteration for sin times. Every iteration would matched all sample images and the previous template, and get a series of flow field. the process above consumes too much computing resources and time.

The steps of VBM-DARTEL are been done as following. (1) Manual reorientation, all images are manually approximately aligned with MNI space to ensure the images were all aligned within about 5cm and about 20 degrees of the template data released with SPM. (2) Segmentation. During segmentation, the scans were bias corrected and normalized, GM, WM and CSF images of the subjects were generated. (3) Templates Creation, DARTEL toolbox, aim to increase the accuracy of inter-subject alignment by modeling the shape of each brain using millions of parameters, was used to create customized template. (4) Normalization to MNI Space, modulated GM, WM and CSF maps were normalized to MNI atlas space as 1.5mm* 1.5mm*1.5mm voxels and a 8 mm full-width at half maximum (FWHM) Gaussian kernel was used for image smoothing. After these steps smoothed modulated normalized maps which represent the regional volume of GM, WM and CSF were obtained to be used for the statistical analysis.

### *C. Statistical analysis*

The modulated GM data of optimized VBM and DARTEL were analyzed using a voxel-wise statistical parametric mapping. Two-sample t-tests for two group comparison were calculated, the threshold for the results reported was $p < 0.005$ and $K>50$ without correction. In order to analysis the result of GM atrophy region, the significant voxels were overlap on the three-dimensional (3D) rendered brain or the international standard MNI avg152 brain template provided by SPM8 and colored by the amount of t value. T-test resultant images were also viewed in xjView toolbox (people.hnl.bcm.tmc.edu/cuixu/xjView).

## III. RESULT

### *A. The change of the volume*

The volumn of GM,WM and CSF by two methods were found in Table 2.

Table 2 Tissue Volume（Volume unit：ml）

| Groups | Method | GM | WM | CSF | GM% | WM% |
|---|---|---|---|---|---|---|
| Baseline | VBM | 501.8 | 404.8 | 698.5 | 31.2% | 25.2% |
| | DARTEL | 569.3 | 452.9 | 760.4 | 31.9% | 25.4% |
| 3-years | VBM | 458 | 397.7 | 694.4 | 29.5% | 25.6% |
| | DARTEL | 531.9 | 448.5 | 825.8 | 29.5% | 24.8% |

GM%=GM/(GM+WM+CSF) , WM%=WM/( GM+WM+CSF)

Many paper[10] didn’t report the percentage of GM volumn. Howerver, different people have differnet volumn of brain. The volumn of GM could not reflect the reality level of atrophy. Therefore, the authors argue that the percentage of GM volumn should be report. From table 2, we could concluded both method had the same percentage of GM and WM. The 3-years percentage of GM vomlumn was smaller than baseline. Howerver, the two groups had the same percentage of WM vomlumn.

### *B. The camparison of GM images after segmenation*

The author reviewed all the GM images of segmenation .Some images still had skull by the way of optimized VBM method. Furthermore, the effect of some layeres were not ideal. On the other hand,the segmented images of DARTEL method could get better results. In the case of AD001 patients,fig 4 showed the C1 view of optimized VBM,fig 5 showed the C1 view of DARTEL.

*C. Analysis of GM atrophy*

The significant voxels overlap on the 3D render and slice view by the way of optimized VBM is showed in fig 6. Fig 7 showed the slice view and render view of DARTEL. From two views,we could see the brain region of optimized VBM were generally in agreement with the DARTEL method. But the GM atrophy of optimized VBM groups is smaller than that of DARTEL’s groups.

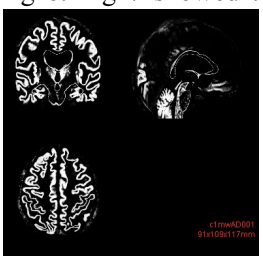

Figure 4 the C1 view of optimized VBM

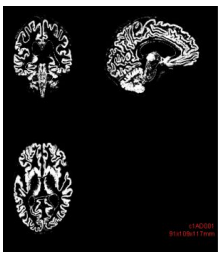

Figure 5 C1 view of DARTEL

## IV. DISCUSSION

Comparing two method,we could concluded that optimized VBM didn’t need AC adjust brfore segment ation. So some C1 images still have some skull after segmentation. Therefore ,it would bring some deviations to the subsequent data processing. While the DARTEL must do AC adjust before segmentation, so C1 images hadn’t skull after segmentnation.

Study from the algorithm, optimized VBM approach only about 1000 parameters. It unable model detailed deformations. While DARTEL have 7 million parameters, the main route is use non-line deformation fields and multiple iterations. So it can keep the efficient information as may as possible. From the run time of machine, optimized VBM is faster than DARTEL dozens of times.

Through the experiment,we could see that the anatomical position such as bilateral frontal lobe, right temporal lobe, bilateral superior temporal gyrus, parahippocampa gyrus, right anterior cingulate,right cerebellum anterior lobe are all reported in both methods,

*D. The brain region of GM atrophy*

According to the report from the xjVIEW and used the predefined anatomical masks obtained from the automated anatomical labeling (AAL) [11], GM atrophy regions, the location and MNI coordinates were listed in Table 3.

It show that the volumetric reduction in these regions are crucial to dignose AD. This result is basically consistent with Huifang Yang’s[12] study But the size of clusters reported by Dartel method is more than twice larger than the size reported by optimized VBM method. Moreover,the anatomical postions of bilateral parahippocampal, left temporal lobe are not reported in optimized VBM method. The early atrophy of temporal lobe would lead to memory loss in recent. The parahippocampal was a key brian region in circuits involved in spatial navigationand memory. Those regions also reported in Chételat’s[13] and others' studies. Therefore, the volumetric reduction of temporal lobe and parahippocampal are frequently detected in AD patients. The two regions are not reported in optimized VBM method might be owing to the tiny volume of these tissues. Then we could conclude that optimized VBM method can't detect all the regions with volumetric reduction especially in tiny tissues.

To sum up, in the analysis of Alzheimer's MR images,both methods could reveal the grey matter atrophy in early stage. But the DARTEL method is more robust than the optimized VBM’s.

TABEL 3 The Comparisons of two method on location of GM loss regions (uncorrected，P<0.005 K>=50)

| Brain region | optimized VBM protocol | | | | | DARTEL arithmetic | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | MNI coordinates | | | Cluster | Peak intensity | MNI coordinates | | | Cluster | Peak intensity |
| Frontal Lobe_R | -61 | -9 | 23 | 53 | 3.04 | 12 | -9 | -34.5 | 655 | 3.93 |
| Temporal Lobe_R | 50 | -43 | -25 | 162 | 3.3 | | | | 307 | |
| Superior Temporal Gyrus_R | -44 | 1 | -15 | 117 | 3.62 | | | | 290 | |
| ParaHippocampal_R | - | - | - | - | - | | | | 247 | |
| Parahippocampa Gyrus | 28 | -12 | -16 | 103 | 2.82 | | | | 229 | |
| Anterior Cingulate_R | -3 | 42 | -10 | 107 | 3.58 | | | | 229 | |
| ParaHippocampal_L | - | - | - | - | - | | | | 220 | |
| Cerebellum Anterior Lobe_R | 36 | -41 | -29 | 50 | 3.49 | 51 | 45 | -30 | 64 | 3.69 |
| Temporal Lobe_L | - | - | - | - | - | -34 | 13.5 | -25.5 | 179 | 3.00 |
| Superior Temporal Gyrus_L | -5 | 22 | 68 | 75 | 3.65 | | | | 176 | |

“-”:means did not report

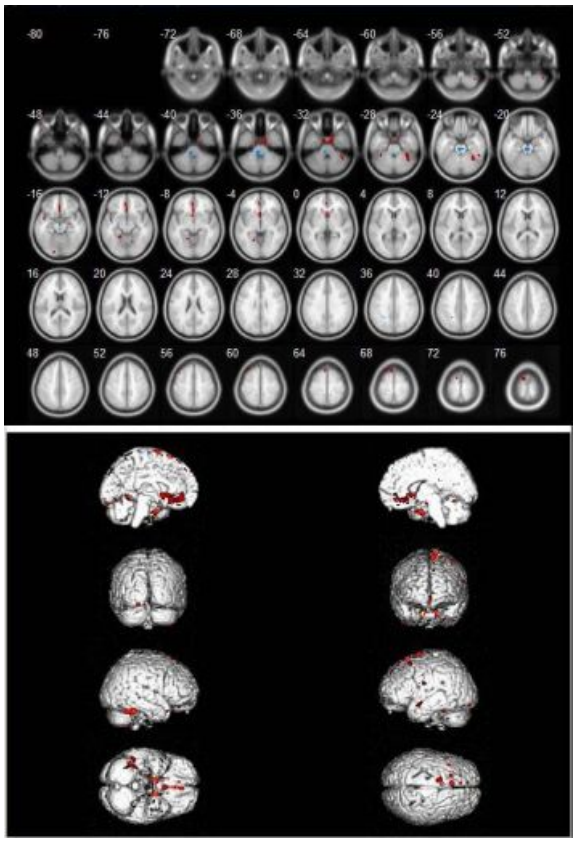

Figure 6 The slice view and render view of optimized VBM

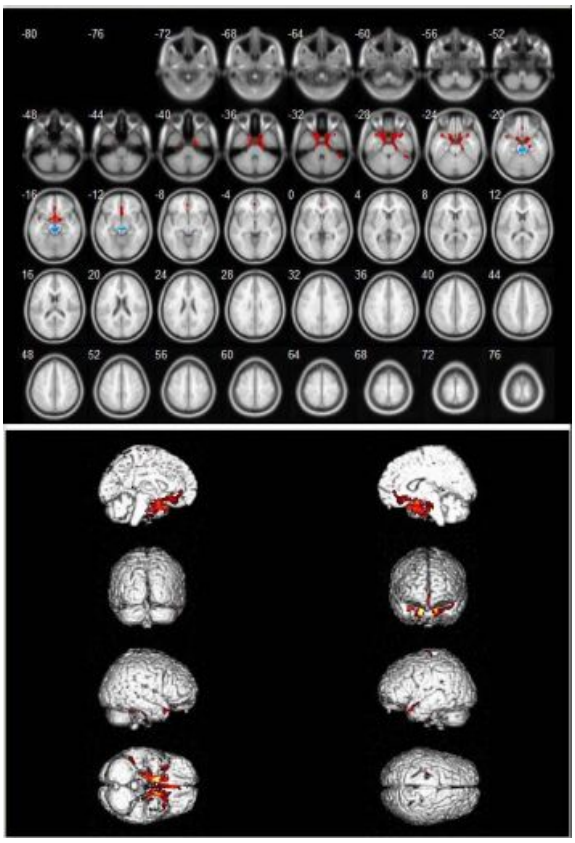

Figure 7 The slice view and render view of DARTEL

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