Comparison of Two Methods
for Automatic Brain Morphometry Analysis

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Abstract. *The methods of computational neuroanatomy are widely used; the data on their individual strengths and limitations from direct comparisons are, however, scarce. The aim of the present study was direct comparison of deformation-based morphometry (DBM) based on high-resolution spatial transforms with widely used voxel-based morphometry (VBM) analysis based on segmented high-resolution images. We performed DBM and VBM analyses on simulated volume changes in a set of 20 3-D MR images, compared to 30 MR images, where only random spatial transforms were introduced. The ability of the two methods to detect regions with the simulated volume changes was determined using overlay index together with the ground truth regions of the simulations; the precision of the detection in space was determined using the distance measures between the centers of detected and simulated regions. DBM was able to detect all the regions with simulated local volume changes with high spatial precision. On the other hand, VBM detected only changes in vicinity of the largest simulated change, with a poor overlap of the detected changes and the ground truth. Taken together we suggest that the analysis of high-resolution deformation fields is more convenient, sensitive, and precise than voxel-wise analysis of tissue-segmented images.*

Keywords

Image registration, voxel-based morphometry, deformation-based morphometry, simulated deformations, MRI.

1. Introduction

Analysis of brain morphology using neuroimaging data is an important area of research in neuroscience. At first volumetric approaches based on manual delineation of regions of interest were used, later followed by several computational approaches. These were designed to overcome limitations of volumetry that is labor intensive (limits the number of subjects in a study), requires a prior anatomical hypothesis for region selection, is prone to errors that arise from subjectivity of boundaries detection (limits

reliability and inter-center comparability of the results), etc. The methods of computational neuroanatomy are widely used now; the data on their individual strengths and limitations from direct comparisons are, however, scarce.

The first implementations of computational neuroanatomic approaches were methods for voxel- and deformation-based morphometry [1], [2]. Voxel-based morphometry (VBM) is based on the assumption that after the removal of general shape differences during image registration local misregistrations remain resulting in between-subject differences in local brain tissue content (usually, the brain intensity image is dissected into different brain tissue compartments which are then analyzed separately). These local differences in tissue content are then explained by a disease effect. The VBM approach was validated several times – corresponding findings were obtained using both VBM and volume calculation [3]-[5], VBM was able to detect focal anatomical lesions [6]. However, the idea of VBM was criticized for its proneness to errors and false positive results due to imprecise and possibly erroneous image registrations [7]. For example group differences of cingulate gyrus observed with VBM were not detected using volumetry - false positive findings resulted from cingulate gyrus shape differences [8].

The magnitude of voxel size changes during the registration process is encoded in the relevant deformation field. Its analysis is the core principle of Deformation-based morphometry (DBM). It is able to detect changes in brain shape and volume irrespective of the brain compartment in which they occur, in contrast to VBM. The term "Deformation-based morphometry" (DBM) was used for the first time by Ashburner [1] to describe a method for detecting global shape changes among the brains of different populations. Later, several other implementations emerged. In general, DBM approaches differ in the registration method used, mainly in terms of the spatial deformation model. Initially, smooth parametric transforms with low-frequency sine basis functions were used [1], [2]. Therefore it was not possible to encode all anatomical variability, including subtle differences, into the spatial transforms (for convenience we will refer to these approaches as "low-resolution DBM"). A complex description of brain morphology has been possible since methods

for high-resolution deformable registration were introduced ("high-resolution DBM"). These methods include spatial deformation models based on high-dimensional parametric transforms [9] or models inspired by similarity to continuum mechanics [10]. There are several ways of deformation field analysis, among them a univariate analysis applied to Jacobian determinants, which represent the factors by which the deformation expands or shrinks volumes near the respective voxels, allows for the detection of local volume changes in the brain. DBM approach was also compared to traditional volume measures and yielded corresponding results [11].

In short, DBM analyzes how much the volume of voxels changed during subject image registration to the template image, in contrast to VBM which focuses on the residual image variability after its transformation. The finer the image transformation, the higher resolution of the deformation field, the more anatomical information is encoded in the deformation field, and the smaller the residual differences in tissue content. The high-resolution DBM could, therefore, encode local anatomical changes; moreover, it focuses on changes in spatial arrangement of images, not on the residual misregistrations, and, therefore, high-resolution DBM could overcome VBM limitations.

We have developed an application of high-resolution deformation-based morphometry with an underlying registration method based on a spatial deformation model which allows for large deformations while preserving the topology of the images. It was able to register brain images with submillimeter precision in a simulation based on synthetic deformation [12]. Such precision could provide high spatial resolution to detect local changes of brain morphology, not only overall changes of brain shape. Indeed, indirect comparison of results obtained using VBM and our DBM method showed that DBM was able to detect changes in first-episode schizophrenia [12] that were analogous to those detected with VBM [13]. That is, high-resolution DBM can detect changes on the similar spatial scale that VBM can.

The aim of the present study was direct comparison of high-resolution DBM with widely used VBM analysis. We expected DBM to find local changes similar to that obtained using VBM.

2. Methods

2.1 Simulated Image Data

We generated two sets of spatial deformations: 1) simulations of normal anatomical variability and 2) simulations of local volume changes at particular stereotactic coordinates. The nonlinear spatial transformations, which represented normal anatomical variability, were computed in our model by natural neighbor scattered data interpolation from random forces pointed in 294 locations in the volume delimited by a binary head mask.

Randomness of the simulator consisted in directions of the forces, magnitudes of the forces, locations of the forces and in leaving out a portion of the forces. We then generated 50 3-D MR brain images by warping a single subject MRI anatomical template from Simulated Brain Database using those deformations. In addition, 20 images contained three volume expansions of different extent in three exactly defined locations, together with the simulated normal anatomical variability. The extent and shape of the volume expansions in each image were randomized to simulate the variability of volume changes in pathological processes. Quantitative parameters of simulated expansions are given in Tab. 1. The other 30 images were generated with the use of deformations which contained only the simulated normal anatomical variability. Displacement vectors in all 50 deformations reached maximum absolute values of about 5 mm.

	T < -4.8263 (FDR 1%)		T < -4.2414 (FDR 5%)		T < -3.5051 (p<0.1%)	
	[mm³]	det($\mathbf{J}$): mean; max	[mm³]	det($\mathbf{J}$): mean; max	[mm³]	det($\mathbf{J}$): mean; max
Exp1	3656	1.7202; 8.3393	4339	1.6663; 8.3393	5538	1.5282; 8.3393
Exp2	883	1.5767; 8.0928	1028	1.5239; 8.0928	1284	1.4557; 8.0928
Exp3	620	1.4227; 7.6176	801	1.3672; 7.6176	1192	1.2939; 7.6176

Tab. 1. Quantitative parameters of simulated expansions. Volume of the simulated expansions was computed from the results of the statistical analysis performed on simulated deformations that contained only the 20 images with three exactly localized volume expansions of different extent. Since there was variability introduced into these deformations, different statistical thresholds provide different volume sizes (based on the power to detect certain effect size given the variability of the data). Exp1-3: Expansion 1-3; det($\mathbf{J}$): mean; max are the mean and maximal relative volume enlargement in significant voxels.

2.2 Deformation-Based Morphometry

The images were corrected for intensity nonuniformity artifacts using an automatic method [14] and then brought into the stereotaxic Talairach space using nine-parameter affine transforms, which were found with the use of an optimal linear registration algorithm [15]. Corrected images were resampled using a trilinear interpolation to contain 1mm × 1mm × 1mm voxels (the 3-D array dimension was 181 × 217 × 181 voxels). The intensity values were linearly rescaled to unsigned 8-bit integers. After these preprocessing steps, all images were visually inspected for large misregistration errors and intensity artifacts. Then our high-dimensional deformable registration method was used to perform DBM. We briefly summarize this algorithm next. Details can be found in [12].

The registration method operates directly on image intensity values with no data reduction by segmentation or classification. The 3-D displacement field which maximizes global mutual information between a reference

image and a floating image is searched in an iterative process that involves computation of local forces as a gradient of point similarity measures and their regularization using the spatial deformation model. The regularization involves two Gaussian spatial filters which form the combined elastic-incremental model introduced in Rogelj et al. [16]. The first spatial filter regularizes displacement improvements which are proportional to applied forces. These displacements are integrated into the final deformation, which is done iteratively by summation. The second part of the model represents the property of elastic materials in which displacements wane after forces are retracted. This is ensured by a second Gaussian smoother. The resulting deformations preserve the topology of the images, i.e. only one-to-one mappings, termed diffeomorphic, are obtained. This requirement is satisfied by controlling the standard deviations of the Gaussian filters which affect the behavior of the spatial deformation model. The standard deviations are incremented each time the minimum Jacobian determinant drops below a predefined threshold. The deformation should capture subtle anatomical variations among studied images; therefore the standard deviations of the Gaussians are decremented as well, whenever the minimum Jacobian determinant starts growing during the registration process.

2.3 Voxel-Based Morphometry

Images were processed according to standard voxel-based morphometry protocol [2] to obtain gray, white matter, and cerebrospinal fluid volume images. We used VBM 5 toolbox (http://dbm.neuro.uni-jena.de/vbm/) implemented in SPM 5 framework (http://www.fil.ion.ucl.ac.uk/spm/). Individual processing steps involved image registration to the standard SPM5 T1 template, tissue segmentation [17] with application of spatial constrains using Hidden Markov Random Field model [18] to minimize the noise level in segmented images, modulation with the determinant of Jacobian to account for changes of local volumes during the registration step, and to obtain images of local tissue volumes, and finally smoothing out of the modulated images with 6 and 12 mm FWHM Gaussian kernel to enable inter-subject comparisons and to render the distribution of the data more normal. Total volume of gray matter, white matter and cerebrospinal fluid were obtained to compute total intracranial volume that was used in subsequent statistical analysis to control for individual differences in brain size.

2.4 Statistical Analysis

Simulated datasets were analyzed using voxel-wise two-sample t-tests in the case of DBM and voxel-wise ANCOVA design with parameters Group as fixed factor and Total intracranial volume as covariate. It is not necessary to correct for individual differences in the brain size in the case of DBM since they are already encoded in the deformation fields.

To compare the results, we computed the overlap between the regions of simulated expansions and the regions detected by DBM and by VBM. We also computed distances between centers of mass of the regions as another way of precision estimation. The regions were delineated by significance thresholding in the t-statistic maps.

3. Results

DBM analysis of the simulated data detected all three regions of local volume expansion. Clusters of significant voxels overlaid the regions of the simulated expansions from 49.4% (smallest expansion and the most stringent statistical threshold applied – $p < 0.01$ FDR corrected) to 92.9% (the medium size expansion, $p < 0.01$ FDR corrected) – for detailed results see Tab. 2. The frequency of false positive voxels ranged from 53.4% (the medium size expansion, $p < 0.05$ FDR corrected) to 17.3% (the smallest expansion, $p < 0.01$ FDR corrected) – see Tab. 2. The distance between the centers of mass of simulated and detected expansions was between 1.42 mm and 3.14 mm – see Tab. 2.

	T< (FDR 1%)			T< (FDR 5%)		
	VBM-6	VBM-12	DBM	VBM-6	VBM-12	DBM
Overlay inx						
Exp1	0 %	0 %	87.7%	0.05 %	0 %	86.8 %
Exp2	0 %	0 %	92.9%	0 %	0 %	92.8%
Exp3	0 %	0 %	49.4%	0 %	0 %	61.8%
E_{FP}						
Exp1	100 %	100 %	44.9 %	60 %	100 %	41.7 %
Exp2	100 %	100 %	49.3 %	100 %	100 %	53.4 %
Exp3	100 %	100 %	17.3 %	100 %	100 %	25.3 %
$|COM\text{-}COM_{ref}|$ [mm]						
Exp1	-	11.41	2.93	7.0	12.18	2.85
Exp2	-	-	2.66	12.0	-	3.14
Exp3	-	-	1.42	12.9	-	1.54

Tab. 2. Results of the analyses of the simulated data. VBM-6: VBM with 6 mm FWHM Gaussian smoothing. VBM-12: VBM with 12 mm FWHM smoothing. Overlay Inx: Overlay index is a ratio of voxels in the region with simulated expansion overlaid by significant voxels from VBM or DBM analysis at different statistical thresholds. E_{FP}: False positive errors, a ratio of significant voxels outside of the simulated expansion. $|COM\text{-}COM_{ref}|$ [mm]: distance between centers of mass of simulated and detected expansions – expressed by Euclidean distance in mm.

On the other hand, VBM analysis was able to detect only one significant change in tissue density that lay in near vicinity to the largest simulated expansion region. The detected region, however, did not overlap with the simulated one at the default statistical threshold ($p < 0.05$ FDR corrected). Losing the significance threshold did the detected region and the ground truth partially overlap – see the results in detail in Tab. 2. The spatial relationship between the largest simulated expansion and two detected regions with DBM and VBM can be inspected in Fig. 1. The results were similar for both 6 mm and 12 mm smoothing performed in VBM. Using gray matter volume

images without smoothing resulted in the failure to detect any changes at any significance threshold used.
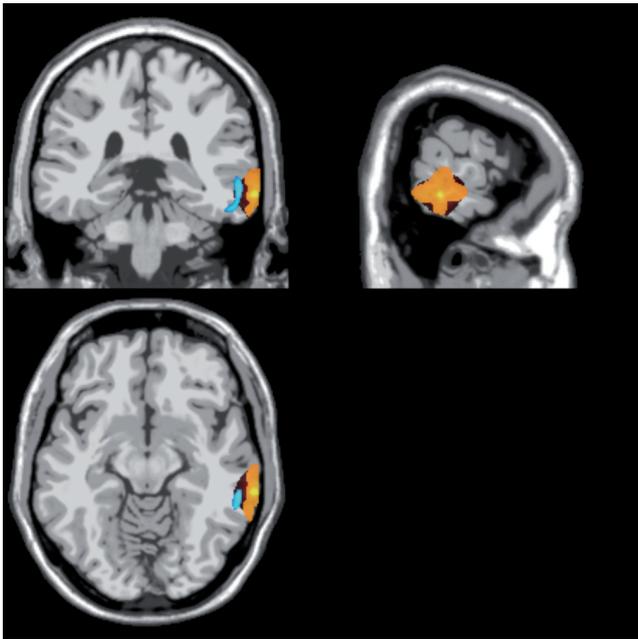

Fig. 1. Spatial relationship between the region of the largest simulated local volume expansion and the regions detected by VBM and DBM. Simulated expansion region (orange) and the regions detected using DBM (red) and VBM (blue).

4. Discussion

We performed a comparison of the performance of newly developed high-resolution deformation-based morphometry with the standard voxel-based morphometry. The analysis of simulated data showed superior performance of DBM that was able to detect all simulated local tissue expansions with very high precision – with the smallest simulated volume expansion at the scale of 600 mm³. VBM was not able to detect any of the three expansions - it was able to uncover tissue density change in near vicinity of the largest expansion – at the scale of 4000 mm³.

This displacement, see Fig. 1, was not affected by the amount of smoothing – similar displacement was found for both 6 and 12 mm FWHM kernels. Moreover, we would rather expect large clusters that cover the simulated abnormality, together with many false positive voxels in the neighborhood, but not displacement of the results away from the simulation, if this shift is due to the smoothing of images. On the other hand, the smoothing is essential for VBM method, both conceptually and practically: it is necessary for intersubject comparisons; zero smoothing prevented detection of changes even at non-significant thresholds.

This displacement of the results obtained using VBM is of critical importance for the validity of evidence for neuroanatomical changes in neuropsychiatric disorders.

For example, in schizophrenia research there is high variability of the spatial localization of gray matter changes reported in individual VBM studies [19], with relatively small overlap of the spatial maps [20]. Usually, this is interpreted in the light of neurobiological heterogeneity of the disorder. Based on our results it seems likely that at least a part of this variability is due to the VBM imprecision. The power of VBM is another issue – even a study with large sample size (400 subjects) failed to find any changes in local gray matter volume in schizophrenia – due to large variability of the data [21].

There are several methodological features that affect the performance of DBM. Of critical concern is to ensure that the deformation does not destroy the brain anatomy, i.e. create non-existing structures, concatenate separate structures etc. Such problems require careful management, especially with regard to registration algorithms based on nonlinear spatial transforms such as those based on viscous fluid dynamics. Therefore various constraints based on topology preservation [22], volume preservation [23] and tissue mass preservation [24] have been used. The ability of DBM to detect local changes of brain anatomy is linked with the dimensionality of the registration method. Our DBM method is based on an original high-dimensional, diffeomorphicity preserving registration technique [12].

The simulated volume changes were not uniform in every subject. They differed in size and shape, which we think is more similar to real volume changes, where the pathological process affects every individual differently. Although DBM results overlapped very well with the simulated tissue changes, they tended to cover larger an area of brain outside the simulation. This might be due to the smoothing effect during the registration step that was necessary in some cases to assure diffeomorphicity.

We believe that the poor performance of VBM, especially in the case of detection of subtle local changes, is caused by the preprocessing steps: a substantial portion of variability is removed with nonlinear registration of the images to the template as well as with Gaussian smoothing of the binary tissue segments. In contrast, when using DBM, one tries to make all variability encoded in the deformation fields. Thus, no trade-off between removing variability with registration and detecting variability itself is necessary.

We think that DBM has several advantages: 1) the analyzed parameter (change of local volume) has a clear biological meaning. On the other hand, in VBM the meaning of tissue density multiplied by local volume change (determinant of Jacobian modulated tissue images), usually interpreted as "tissue volume" is much less evident; 2) the changes are always detected in the context of whole brain morphology described by high-resolution deformation fields; 3) the localization of the changes is evident from their position within the brain. There is no risk of mirror changes or the question of what tissue is affected. Today, most VBM studies analyze only one tissue - usually gray

matter. However, when no information is provided about the corresponding changes in WM and CSF, it is not possible to draw clear conclusions; 4) as suggested by our simulation, it seems that DBM could have higher spatial precision and higher sensitivity to detect subtle local volume changes.

5. Conclusion

We have demonstrated that high-resolution deformation based morphometry is 1) able to detect local changes of brain morphology, 2) with high spatial precision, and 3) with sufficient power in a sample, which size resembles usual clinical samples. In contrast to these features of DBM, VBM was not powerful enough to detect any simulated changes, and the changes found by VBM at a non-significant threshold were shifted away. These findings suggest that the heterogeneity of results found by VBM in many neuropsychiatric disorders including schizophrenia may be caused by methodological faults in part, not only by the possible neurobiological heterogeneity. Taken together we suggest that the analysis of high-resolution deformation fields is more convenient and precise than voxel-wise analysis of tissue-segmented images.

Acknowledgements

References

[1] ASHBURNER, J., HUTTON, C., FRACKOWIAK, R., JOHNSRUDE, I., PRICE, C., FRISTON, K. J. Identifying global anatomical differences: deformation-based morphometry. *Hum Brain Mapp*, 1998, vol. 6, p. 348 - 357.

[2] ASHBURNER, J., FRISTON, K. J. Voxel-based morphometry--the methods. *Neuroimage*, 2000, vol. 11, p. 805 - 821.

[3] GIULIANI, N. R., CALHOUN, V. D., PEARLSON, G. D., FRANCIS, A., BUCHANAN, R. W. Voxel-based morphometry versus region of interest: a comparison of two methods for analyzing gray matter differences in schizophrenia. *Schizophr Res*, 2005, vol. 74, p. 135 - 147.

[4] GONG, Q. Y., SLUMING, V., MAYES, A., KELLER, S., BARRICK, T., CEZAYIRLI, E., ROBERTS, N. Voxel-based morphometry and stereology provide convergent evidence of the importance of medial prefrontal cortex for fluid intelligence in healthy adults. *Neuroimage*, 2005, vol. 25, p. 1175 - 1186.

[5] KELLER, S. S., MACKAY, C. E., BARRICK, T. R., WIESHMANN, U. C., HOWARD, M. A., ROBERTS, N. Voxel-based morphometric comparison of hippocampal and extrahippocampal abnormalities in patients with left and right hippocampal atrophy. *Neuroimage*, 2002, vol. 16, p. 23 - 31.

[6] MEHTA, S., GRABOWSKI, T. J., TRIVEDI, Y., DAMASIO, H. Evaluation of voxel-based morphometry for focal lesion detection in individuals. *Neuroimage*, 2003, vol. 20, p. 1438 - 1454.

[7] BOOKSTEIN, F. L. Voxel-based morphometry should not be used with imperfectly registered images. *Neuroimage*, 2001, vol. 14, p. 1454 - 1462.

[8] CORBO, V., CLEMENT, M. H., ARMONY, J. L., PRUESSNER, J. C., BRUNET, A. Size versus shape differences: contrasting voxel-based and volumetric analyses of the anterior cingulate cortex in individuals with acute posttraumatic stress disorder. *Biol Psychiatry*, 2005, vol. 58, p. 119 - 124.

[9] XIE, Z., FARIN, G. E. Image registration using hierarchical B-splines. *IEEE Trans Vis Comput Graph*, 2004, vol. 10, p. 85 - 94.

[10] CSERNANSKY, J. G., WANG, L., JONES, D., RASTOGI-CRUZ, D., POSENER, J. A., HEYDEBRAND, G., MILLER, J. P., MILLER, M. I. Hippocampal deformities in schizophrenia characterized by high dimensional brain mapping. *Am J Psychiatry*, 2002, vol. 159, p. 2000 - 2006.

[11] GASER, C., NENADIC, I., BUCHSBAUM, B. R., HAZLETT, E. A., BUCHSBAUM, M. S. Deformation-based morphometry and its relation to conventional volumetry of brain lateral ventricles in MRI. *Neuroimage*, 2001, vol. 13, p. 1140 - 1145.

[12] SCHWARZ, D., KASPAREK, T., PROVAZNIK, I., JARKOVSKY, J. A deformable registration method for automated morphometry of MRI brain images in neuropsychiatric research. *IEEE Trans Med Imaging*, 2007, vol. 26, p. 452 - 461.

[13] KASPAREK, T., PRIKRYL, R., MIKL, M., SCHWARZ, D., CESKOVA, E., KRUPA, P. Prefrontal but not temporal grey matter changes in males with first-episode schizophrenia. *Prog Neuropsychopharmacol Biol Psychiatry*, 2007, vol. 31, p. 151 to 157.

[14] SLED, J. G., ZIJDENBOS, A. P., EVANS, A. C. A nonparametric method for automatic correction of intensity nonuniformity in MRI data. *IEEE Trans Med Imaging*, 1998, vol. 17, p. 87 - 97.

[15] COLLINS, D. L., NEELIN, P., PETERS, T. M., EVANS, A. C. Automatic 3D intersubject registration of MR volumetric data in standardized Talairach space. *J Comput Assist Tomogr*, 1994, vol. 18, p. 192 - 205.

[16] ROGELJ, P., KOVACIC, S. Spatial deformation models for non-rigid image registration. In *Proceedings of the 9th Computer Vision Winter Workshop (CVWW'04)*. Piran (Slovenia), p. 79 - 88.

[17] ASHBURNER, J., FRISTON, K. J. Unified segmentation. *Neuroimage*, 2005, vol. 26, p. 839 - 851.

[18] CUADRA, M. B., CAMMOUN, L., BUTZ, T., CUISENAIRE, O., THIRAN, J. P. Comparison and validation of tissue modelization and statistical classification methods in T1-weighted MR brain images. *IEEE Trans Med Imaging*, 2005, vol. 24, p. 1548 - 1565.

[19] HONEA, R., CROW, T. J., PASSINGHAM, D., MACKAY, C. E. Regional deficits in brain volume in schizophrenia: a meta-analysis of voxel-based morphometry studies. *Am J Psychiatry*, 2005, vol. 162, p. 2233 - 2245.

[20] ELLISON-WRIGHT, I., GLAHN, D. C., LAIRD, A. R., THELEN, S. M., BULLMORE, E. The anatomy of first-episode and chronic schizophrenia: an anatomical likelihood estimation meta-analysis. *American Journal of Psychiatry*, 2008, vol. 165, p. 1015 - 1023.

[21] MEDA, S. A., GIULIANI, N. R., CALHOUN, V. D., JAGANNA-THAN, K., SCHRETLEN, D. J., PULVER, A., CASCELLA, N., KESHAVAN, M., KATES, W., BUCHANAN, R., SHARMA, T., PEARLSON, G. D. A large scale (N=400) investigation of gray matter differences in schizophrenia using optimized voxel-based morphometry. *Schizophr Res*, 2008, vol. 101, p. 95 - 105.

[22] ASHBURNER, J. A fast diffeomorphic image registration algorithm. *Neuroimage*, 2007, vol. 38, p. 95 - 113.

[23] ROHLFING, T., MAURER, C. R., JR., BLUEMKE, D. A., JA-COBS, M. A. Volume-preserving nonrigid registration of MR breast images using free-form deformation with an incompressibility constraint. *IEEE Trans Med Imaging*, 2003, vol. 22, p. 730 to 741.

[24] SHEN, D., DAVATZIKOS, C. Very high-resolution morphometry using mass-preserving deformations and HAMMER elastic registration. *Neuroimage*, 2003, vol. 18, p. 28 - 41.

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