CORRESPONDENCE EVALUATION IN LOCAL SHAPE ANALYSIS AND STRUCTURAL SUBDIVISION

Martin Styner[1,2], *Shun Xu*[1], *Mohammed El-Sayed*[3], *Guido Gerig*[1,2]

Depts. of Computer Science[1] and Psychiatry[2], University of North Carolina, Chapel Hill, USA
Dept. of Psychiatry[3], Mansoura University, Mansoura, Egypt

ABSTRACT

Regional volumetric and local shape analysis has become of increasing interest to the neuroimaging community due to the potential to locate morphological changes. In this paper we compare three common correspondence methods applied to two studies of hippocampal shape in schizophrenia: correspondence via deformable registration, spherical harmonics (SPHARM) and Minimum Description Length (MDL) optimization. These correspondence methods are evaluated in respect to local statistical shape analysis and structural subdivision analysis. Results show a non-negligible influence of the choice of correspondence especially in studies with low numbers of subjects. The differences are especially striking in the structural subdivision analysis and hints at a possible source for the diverging findings in many subdivision studies. Our comparative study is not meant to be exhaustive, but rather raises awareness of the issue and shows that assessing the validity of the correspondence is an important step.

Keywords: Image shape analysis, Shape, Shape measurement, Brain

1. INTRODUCTION

Quantitative brain morphologic assessment is often based on volumetric changes, as they may explain atrophy or dilation due to illness. On the other hand, structural changes at specific locations are not sufficiently reflected. Shape analysis has thus become of increasing interest to the neuroimaging community due to its potential to precisely locate morphological changes between healthy and pathological structures.

A key step in shape analysis involves establishing a correspondence between shape descriptions of different objects. Unfortunately there is no generally accepted definition for the *correct* localized correspondence in biological structures. It is thus difficult to evaluate different correspondence methods [1] and current shape analysis studies in technical and medical literature mainly assume a negligible influence of the choice of correspondence. In contrast to shape modeling[1], no comparison studies of correspondence for *group difference testing* have been published so far.

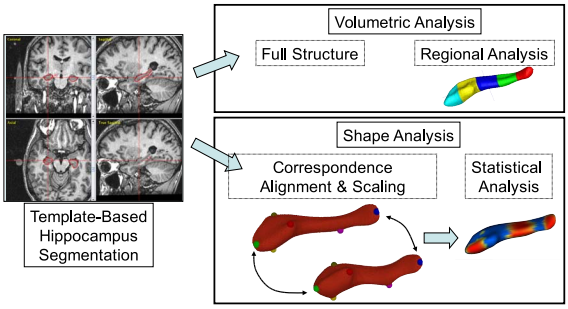


Fig. 1. Schematic view of the proposed analysis.

Starting with D'Arcy [2] in his ground-breaking book *On Growth and Form*, researchers have developed methods for the assessment of 2D and 3D shape. The proposed methods focused on landmarks [3], densely sampled Point Distribution Models (PDM) [4], spherical harmonics (SPHARM) [5], the SPHARM implied PDM [6, 7], and medial descriptions [8, 9]. Several automatic correspondence approaches have been proposed for PDMs based on geometry [10, 11] and on population statistics [12, 13]. Also, shape analysis via template deformation was proposed [14, 15] with correspondence mainly depending on matching and regularization criterions.

In this paper we investigate the influence of 3 selected correspondence methods on local shape and regional subdivision analysis. These methods are presented in more detail in the next section, followed by their results in 2 shape studies.

2. MATERIALS AND METHODS

This section describes the methods we applied in our comparison study (see Fig 1). MR images were first segmented using deformable registration, which establishes the first correspondence. The surfaces are converted into sampled spherical harmonics (SPHARM-PDM), the second correspondence. Using this correspondence as initialization, the Minimum Description Length(MDL) correspondence is computed. Our shape

Thanks to C. Brechbühler for the original SPHARM software, to S. Joshi for the deformation tool, and to C. Taylor and R. Davies for the MDL software. This research is supported by NIH grants P01 EB002779, UNC Neurodevelopmental Disorders Research Center HD 03110 and Roadmap Grant U54 EB005149-01, National Alliance for Medical Image Computing.

testing procedure and template-based subdivision is then applied to all methods. For reasons of clarity, we focus on the analysis of the right hippocampus. Similar result were observed on the left hippocampus.

Subjects and Image Acquisition: The first study examines hippocampal morphometry in adolescent schizophrenia with 15 schizophrenic subjects (age: 15.72y (2.47), gender m/f: 80%/20%, duration of illness: 2.72y (2.75)) and 17 control subjects (age 15.88y (2.08), gender m/f: 42%/58%). The number of samples is low, but such sample sizes are not uncommon in small scale clinical studies. The second study examines hippocampal morphometry in adult schizophrenia [6]. 54 schizophrenis subjects (age: 30.1y (11.9), only male) and 26 healthy control (age: 31.2y (10.7), only male) subjects were analyzed. The groups are matched for age and ethnicity. All subjects were scanned on the same 1.5 T scanner and with the same protocol (IR-Prepped SPGR, axial, 0.9375x0.9375x1.5mm^3).

Correspondence via Deformable Registration: Our method for hippocampal segmentation is based on a deformable registration of a template to each subject's MRI[15]. The registration is performed in three steps: intensity normalization, manual landmark selection and deformable registration. Using 26 landmarks, a template hippocampus image is deformably registered in a coarse to fine procedure. The deformation is then applied to the template's hippocampus surface. Intra-rater reliability of the resulting volumes was at 0.90. All segmentations were performed by the same, blinded rater (ME). The resulting correspondence is influenced by the grayscale image intensities, the hippocampal landmarks and the shape of the template hippocampus (see Figure 2A). It is important to note that this correspondence is a volumetric correspondence rather than a boundary correspondence and we present an analysis of the boundary correspondence only.

Correspondence via SPHARM-PDM: The SPHARM-PDM description is a hierarchical, global boundary description that only represents objects of spherical topology ([5]). A spherical parameterization is computed via optimizing an equal area mapping of the 3D voxel mesh onto the unit sphere and minimizing angular distortions. A set of coefficients, which weight spherical harmonic basis functions, are fitted to the 3D voxel mesh. Truncating the spherical harmonic series at different degrees results in representations at different levels of detail. Truncating it at the first degree will result in an ellipsoid, whose axis are employed for aligning the spherical parameterizations. The parameterization thus directly defines the correspondence across different objects (see Figure 2B). It is evident that the correspondence of objects with rotational symmetry in the first order ellipsoid is ambiguously defined. Based on a uniform icosahedron-subdivision of the spherical parameterization, we obtain a Point Distribution Model (PDM) at any desired subdivision level.

Correspondence via MDL: Kotcheff [12] and later Davies [13] proposed to use an optimization process that assigns the

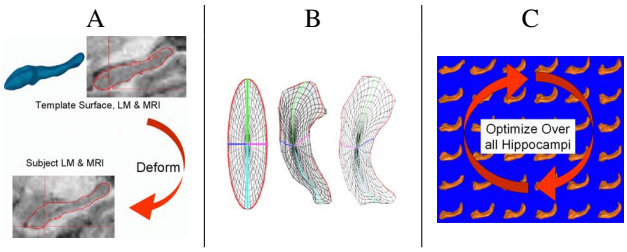
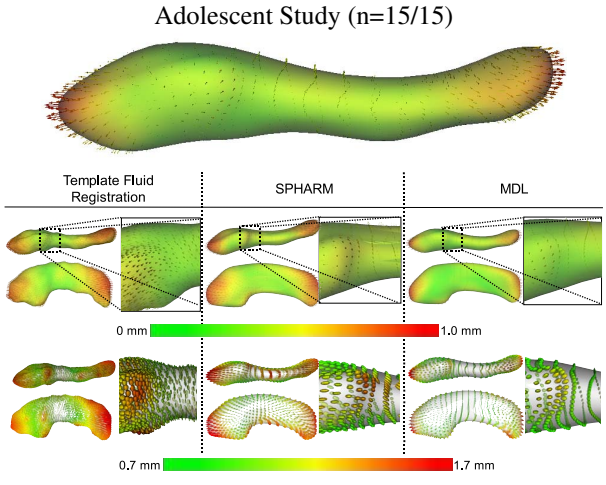


Fig. 2. A: Template deformation correspondence. B: SPHARM by parametrization alignment in first order ellipsoid. C: Optimization of MDL over object population.

best correspondence. Every object's correspodence in a population is iteratively changed while minimizing a population-wise metric (see Figure 2C). Davies proposed the use of the Minimum Description Length (MDL) metric suggesting that the best correspondences are those that build an optimally compact statistical Principal Component Analysis shape model [16]. MDL balances the model complexity, expressed in terms of the model parameters, against the quality of fit between the model and the data. The computation of the statistical model though employs statistical information, which strongly correlates with the covariance information used in our shape testing procedure. It has thus been suggested that a statistical optimistic bias is introduced when using the same MDL training population as the testing population. In this paper, the MDL training population is a set of hippocampi from 20 separate healthy control subjects acquired with the same scanning and segmentation protocol (age range: 20-44y).

Local Shape Analysis: As a prerequisite for any shape analysis, objects have to be normalized with respect to a reference coordinate frame. This normalization is achieved in the presented study using the rigid Procrustes[11] alignment method to an overall mean hippocampus surface and total brain volume scaling normalization. Both SPHARM and registration based correspondence is established independent of the choice of alignment and scale. In contrast, MDL is computed using local surface coordinates and thus depends on a prior alignment and choice of scale.

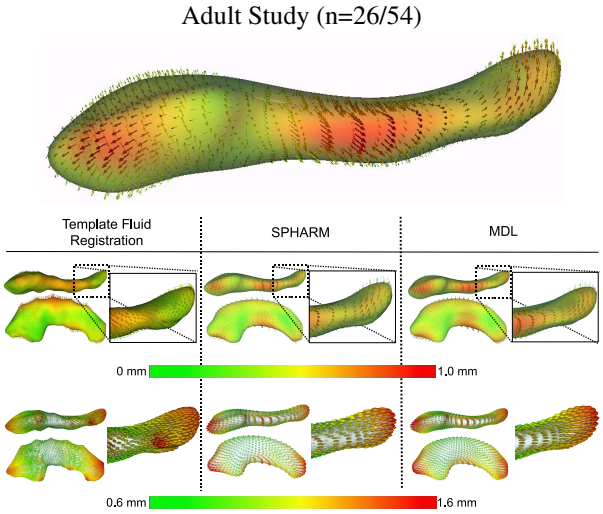
The local shape analysis first computes the mean hippocampal surface points for each group, their local differences, as well as local variability. The differences between the group mean surfaces are visualized color-coded magnitude and difference vectors on the combined mean surface (see Figures 3 and 4). The variability is assessed using the covariance ellipsoid visualization. The local shape hypothesis testing procedure then analyzes the multivariate Hotelling T^2 difference at each location for significance using a non-parametric permutation testing scheme [17, 6]. This results in a raw and corrected P-value significance maps. The first represents an optimistic estimate of the real significance, whereas the latter represents a pessimistic estimate that is guaranteed to control



P-value Table Regional Subdivision

	A head	P head	Body	A tail	P tail
Registration	0.049*	0.048*	0.11	0.68	0.74
SPHARM	0.067	0.043*	0.004**	0.27	0.17
MDL	0.014*	0.11	0.17	0.51	0.01*

Fig. 3. Descriptive population statistics in adolescent schizophrenia study. Top: Magnitude colored mean difference vectors from schizophrenic to control mean using MDL. Middle: Difference and covariance ellipsoid visualizations. Bottom: P-values from the regional subdivision analysis.



P-value Table Regional Subdivision

	A head	P head	Body	A tail	P tail
Registration	0.761	0.391	0.010*	0.202	0.646
SPHARM	0.006**	0.001**	0.009**	0.008**	0.002**
MDL	0.001**	0.001**	0.006**	0.011*	0.001**

Fig. 4. Descriptive population statistics in adult schizophrenia study. Top: Magnitude colored mean difference vectors from schizophrenic to control mean using MDL. Middle: Difference and covariance ellipsoid visualizations. Bottom: P-values from the regional subdivision analysis.

the rate of false positives across the whole hippocampal surface.

Regional Subdivision: The computation of regional volumes based on subdivisions of anatomical brain structures is quite common. Often subdivision protocols are based on landmarks, are executed manually and thus time-consuming, as well as not fully reproducible. Our regional subdivision is based on a prior, medial shape based subdivision template computed on the average hippocampal surface, which is then propagated to each individual hippicampus using the surface correspondence. The template subdivision is defined by the planes orthogonal to a single medial axis [18]. In this study, the medial axis subdivision, which runs roughly along the anterior-posterior direction, results in 5 regions: the hippocampal head (anterior, posterior), body, and tail (anterior,posterior). This subdivision scheme is fully automatic and reproducible.

3. RESULTS

For reasons of clarity, results have been computed without explicitly correcting for age, gender and medication type. An implicit correction is achieved by the normalization with the total brain volume. As a first analysis, hippocampal volumes in both studies were significantly smaller in schizophrenics (adolescent p=0.037; adult p = 0.0013) than in controls.

Mean Difference and Covariance Field: For the adolescent study (see Fig. 3) main differences are located in the anterior head and the posterior tail. A slight bending of the tail and body seems to be present. The registration based correspondence shows larger differences, and higher variability. We observe also that in many areas the difference vectors for SPHARM and the registration based correspondence run along the surface, whereas for MDL the difference vectors are oriented closer towards the surface normal. For the adult study (see Fig. 4), the main differences are similarly seen in the anterior head region, the mid-body and the posterior tail region, with a clear bending of body and tail. The registration based correspondence again produces larger differences, but also shows higher variability. Mean differences and variability seems to agree well across the different methods.

3D Local Shape Analysis: The raw significance maps shown in Figure 5 visualize the differences between the different correspondence methods. While the significance maps for SPHARM and MDL show agreement in the adolescent study and adult study, this is less the case for the registration based correspondence, especially in the adolescent study. Only SPHARM and MDL show a significantly different tail region in the significance maps. Both methods also show the strongest significant difference in the body region, where the mean differences are quite small, but so is the variability. The head region, which shows large mean differences, is less significantly different due to the large variability in that region. The significance maps in the adult study also shows consid-

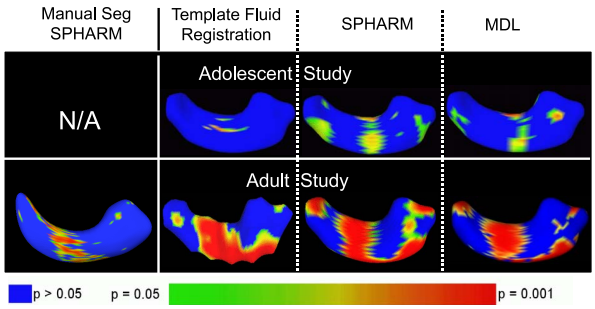


Fig. 5. Local shape analysis: Raw p-value significance maps (blue: no significance, green-red: differences of increasing significance) from superior viewpoint. The significance maps for SPHARM and MDL show good agreement. Moderate agreement is present in the registration based correspondence maps. The full left column shows the significance map using SPHARM correspondence with an alternative manual segmentation method in the adult study. On the inferior side this significance map also shows significance in the tail region.

erable agreement with an additional analysis performed on the same datasets segmented with an alternative fully manual method and SPHARM correspondence[6]. That analysis shows less overall significance due to the higher variability of the segmentation process.

Regional Subdivision Analysis: Due to its cumulative nature, we would expect more stable results in the subdivision analysis. As shown in Figs. 3 and 4, this is not the case. The correspondence methods result in different patterns of significantly different regions, despite the agreement in the local shape analysis. In the adolescent study, the registration based correspondence shows the head region to be moderately significant and a minor trend in the body region. SPHARM correspondence shows the highest significance in the body region and a moderate significance in the posterior head region, as well as trends in the anterior head and posterior tail region. MDL correspondence shows good significance in both the anterior head and posterior tail region, as well as trends in the posterior head and body region. The main agreement between the methods is that the anterior tail region shows no significant difference. In the adult study, SPHARM and MDL show general enlargement in all hippocampal regions, whereas the registration based method only shows an enlarged body.

4. DISCUSSION AND CONCLUSION

In this paper, we show that the choice of correspondence has a non-negligible influence on the analysis of shape and regional volumes. This influence seems to be higher in studies with lower number of subjects. Furthermore, the instability of the regional volume results is astonishing and suggests that analyzing shape is more stable then the regional volumes. We propose that additional means such as mean difference and covariance maps give additional insight relevant to judge the study's validity regarding its choice of correspondence.

The results suggest that the deformable registration based correspondence is less suited for statistical shape analysis. Due to its higher variance, a larger sample size seems necessary to attain the same level of significance as SPHARM and MDL. Furthermore, the correspondence appears noisier and less stable. However, the registration based method determines the correspondence not based on the boundary, but rather by image intensities within and outside of the object. Evaluating such a method on the basis of the boundary shape alone is not entirely fair.

MDL seems to show the most plausible results in the smaller sized adolescent study, whereas there is no clear differences between the methods for the larger adult study. One of the main reasons for the differences between the different correspondence methods could be the relatively low number of samples coupled with the large shape variability due to the high age and gender range in this study of adolescents.

The presented study is by no means complete, but rather based on selected correspondence methods. Our research raises awareness to an important topic that has not been appropriately discussed in the field thus far.

5. REFERENCES

[1] M. Styner, K. Rajamani, L.P. Nolte, G. Zsemlye, G. Szekely, C. Taylor, and R. H. Davies, "Evaluation of 3d correspondence methods for model building," in *IPMI*, July 2003, pp. 63–75.

[2] D. Thomson, *On Growth and Form*, Cambridge University Press, second edition, 1942.

[3] F.L. Bookstein, "Shape and the Information in Medical Images: A Decade of the Morphometric Synthesis," *Comp. Vision and Image Under.*, vol. 66, no. 2, pp. 97–118, May 1997.

[4] T. Cootes, C.J. Taylor, D.H. Cooper, and J. Graham, "Active shape models - their training and application," *Comp. Vis. Image Under.*, vol. 61, pp. 38–59, 1995.

[5] C. Brechbühler, G. Gerig, and O. Kübler, "Parametrization of closed surfaces for 3-D shape description," *Comp. Vision, Graphics, and Image Proc.*, vol. 61, pp. 154–170, 1995.

[6] M. Styner, J.A. Lieberman, D. Pantazis, and G. Gerig, "Boundary and medial shape analysis of the hippocampus in schizophrenia," *Medical Image Analysis*, vol. 8, no. 3, pp. 197–203, 2004.

[7] L. Shen, J. Ford, F. Makedon, and A. Saykin, "Hippocampal shape analysis surface-based representation and classification," in *SPIE-Medical Imaging*, 2003.

[8] S. Pizer, D. Fritsch, P. Yushkevich, V. Johnson, and E. Chaney, "Segmentation, registration, and measurement of shape variation via image object shape," *IEEE Trans. Med. Imaging*, vol. 18, pp. 851–865, Oct. 1999.

[9] S Bouix, JC Pruessner, Collins D Louis, and K Siddiqi, "Hippocampal shape analysis using medial surfaces," *Neuroimage*, vol. 25, no. 4, pp. 1077–89, May 2005.

[10] D. Meier and E. Fisher, "Parameter space warping: Shape-based correspondence between morphologically different objects," *IEEE Transactions on Medical Imaging*, vol. 12, pp. 31–47, 2002.

[11] A. Rangarajan, H. Chui, and F. Bookstein, "The softassign procrustes matching algorithm," in *IPMI*, 1997, number 1230 in LNCS, pp. 29–42.

[12] A.C.W. Kotcheff and C.J. Taylor, "Automatic construction of eigenshape models by direct optimization," *Medical Image Analysis*, vol. 2, no. 4, pp. 303–314, 1998.

[13] R.H. Davies, C.J. Twining, T.F. Cootes, J.C. Waterton, and C.J. Taylor, "A minimum description length approach to statistical shape modeling," *IEEE Trans. Med. Imaging*, vol. 21, no. 5, pp. 525–537, May 2002.

[14] C. Davatzikos, M. Vaillant, S. Resnick, J.L Prince, S. Letovsky, and R.N. Bryan, "A computerized method for morphological analysis of the corpus callosum," *J. of Comp. Assisted Tomography*, vol. 20, pp. 88–97, Jan./Feb 1996.

[15] S. Joshi, M Miller, and U. Grenander, "On the geometry and shape of brain sub-manifolds," *Pat. Rec. Art. Intel.*, vol. 11, pp. 1317–1343, 1997.

[16] T. F. Cootes, A. Hill, C. J. Taylor, and J. Haslam, "The Use of Active Shape Models for Locating Structures in Medical Images," *Image and Vision Computing*, vol. 12, no. 6, pp. 355–366, 1994, Electronic version: http://s10d.smb.man.ac.uk/publications/index.htm.

[17] D. Pantazis, R.M. Leahy, T.E. Nichol, and M. Styner, "Statistical surface-based morphometry using a non-parametric approach," in *Int. Symposium on Biomedical Imaging(ISBI)*, April 2004, In press.

[18] M. Styner, G. Gerig, J. Lieberman, D. Jones, and D. Weinberger, "Statistical shape analysis of neuroanatomical structures based on medial models," *Medical Image Analysis*, vol. 7, no. 3, pp. 207–220, 2003.