HIPPOCAMPAL SHAPE ANALYSIS IN THE LAPLACE BELTRAMI FEATURE SPACE FOR TEMPORAL LOBE EPILEPSY DIAGNOSIS AND LATERALIZATION

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ABSTRACT

Shape analysis plays an important role in many medical imaging studies. One of the recent shape analysis methods uses the Laplace Beltrami operator which is also used in this paper for hippocampal shape comparison. We proposed a feature vector which consists of size measures and shape descriptors based on Laplace Beltrami eigenvalues and eigenfunctions. The aforementioned feature space is utilised for automatic differentiating normal subjects from epileptic patients as well as distinguishing epileptic patients with left temporal lobe epilepsy (LTLE) from patients with right temporal lobe epilepsy (RTLE). Achieved results are diagnostic accuracy of 93% with 95% sensitivity and lateralization accuracy of 86%. The results are comparable to spherical harmonic based shape analysis results and notably improved in comparison to volumetric analysis results.

Index Terms— Hippocampus, Epilepsy disease, Shape analysis, Laplace Beltrami eigenvalues and eigenfunctions, MS complex

1. INTRODUCTION

Studying brain structures for the neurodegenerative diseases is an interesting topic in medical imaging. Some of these prevalent diseases are schizophrenia, Alzheimer's, Parkinson, and epilepsy where there are evidences in the literature [1] showing that the brain structures deform when they occur. So using accurate representatives is beneficial to parameterize the deformation which will help diagnosis of the above-mentioned illnesses automatically.

Early common works were focused on volumetric analysis [2] which is capable of representing this deformation and is easy to interpret. Recently, shape analysis techniques have become more popular since they are more discriminative than volumetric measurements and may provide additional geometric and morphometric features.

Examples of shape descriptors are the shape index, moment invariants, spherical harmonics, spherical wavelets, and Laplace Beltrami operator [3-5, 10]. In most of these methods, the volume or surface is decomposed into series of bases functions, and the resulting coefficients are used as shape features.

This study focuses on epilepsy among different neurodegenerative diseases which damage hippocampus. The used data for this purpose is collected from patients with temporal lobe epilepsy (TLE) which is symptomatic localization-related epilepsy.

Studying the hippocampus of patients with epilepsy has led researches to evaluate changes in the shape of this structure for both statistical shape analysis and shape comparison purposes used for diagnosis and lateralization. Previous shape analysis approaches utilized for epilepsy lateralization, include using kernel Fisher [6], high-dimensional mapping [7], and spherical harmonics [5]. In our previous work [8], we used Laplace Beltrami spectrum as global shape descriptors for epilepsy diagnosis.

Using the Laplace Beltrami operator for shape analysis, through cubic finite element (FE) computations, was first introduced by Reuter et al. [9-10]. In [10], they introduced Laplace Beltrami eigenfunctions for extracting topological features and examined the features capability in discriminating normal subjects and subjects with schizotypal personality disorder.

Advantages of Laplace Beltrami operator over the other methods are as follows. First, the Laplace Beltrami eigenvalues and eigenfunctions are isometry-invariant whereas methods based on spherical harmonics or invariant moments are not. Secondly, a small amount of pre-processing is needed while other methods need registration or alignment.

The contribution of this paper is using both global and local shape descriptors based on Laplace Beltrami operator for both epilepsy diagnosis and lateralization. The rest of the paper is organized as follows: At Section 2, the proposed method and its theoretical background is presented. Section 3 describes the results of classification and investigates the effect of using shape descriptors in addition to common size descriptors. Conclusions are given in Section 4.

2. METHOD

The objective of this study is to compare normal subjects to epileptic patients, as well as patients with left temporal lobe epilepsy (LTLE) to patients with right temporal lobe epilepsy (RTLE). For this purpose we compute three different groups of size and shape descriptors. The volume and the surface area of each hippocampus are measured for size comparison and Laplace Beltrami eigenvalues and eigenfunctions are computed to extract global and local shape descriptors respectively. To study the eigenfunctions topological

methods including the construction of Morse-Smale (MS) complex and zero level set are utilised.

The Laplace Beltrami eigenvalues and eigenfunctions are characteristics proportional to the topology and the geometry of an object. They can be used for comparison of objects such as surfaces and solids, independently from their orientation and as a result minimal pre-processing is needed. This idea was introduced in [9]. Our proposed method consisting of the following general steps is presented in Fig. 1:

1. Pre-processing
2. Computing Laplace Beltrami eigenvalues and eigenfunctions
3. Applying topological methods
4. Measurement of volume and surface area
5. Feature extraction
6. Classification

The only necessary pre-processing steps applied on the manually segmented magnetic resonance (MR) hippocampi are constructing the 3D binary shapes, extracting the triangulated surface and normalizing to unit surface area. The theoretical background of the proposed method is described in the following steps.

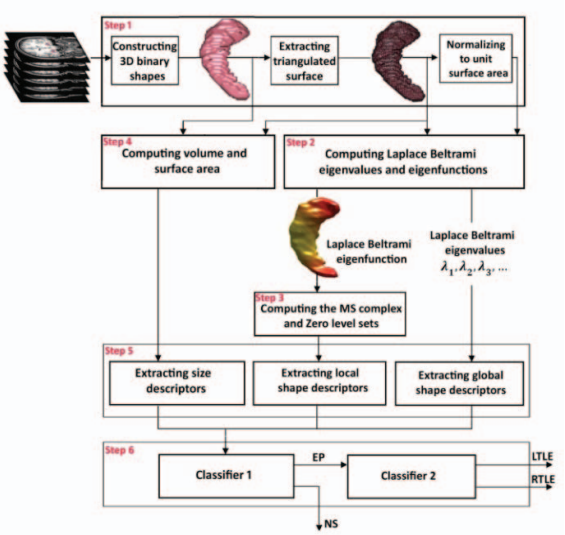


Fig. 1: The proposed procedure for hippocampal shape analysis. The system inputs are classified to normal subjects (NS) and epileptic patient (EP) using classifier 1 and the EPs are classified to patients with left temporal lobe epilepsy (LTLE) and patients with right temporal lobe epilepsy (RTLE).

2.1. The Laplace Beltrami eigenvalues and eigenfunctions

The basic theory of The Laplace Beltrami eigenvalues and eigenfunctions is presented briefly below.

The Laplace Beltrami operator of a smooth function *f* on a Riemannian manifold M is given by

$$\Delta f = div(grad\, f) \tag{1}$$

where *div* and *grad* are divergence and gradient operators on the Riemannian manifold *M*, respectively.

In a local coordinate, if the metric is given by *gij* then the Laplace Beltrami operator of a function is computed by:

$$\Delta f = \frac{1}{W}\sum_{i,j} \partial_i\left(g_{ij} W \partial_j f\right) \tag{2}$$

where

$$g_{ij} = \langle \partial_i \psi, \partial_j \psi \rangle, \qquad G = \left(g_{ij}\right),\ W = \sqrt{\det G},$$

$$\left(g_{ij}\right) \coloneqq G^{-1} \tag{3}$$

It is a well known fact that the Laplace Beltrami operator has a discrete non-negative spectrum diverging to infinity:

$$0 \le \lambda_1 \le \lambda_2 \le \cdots \uparrow \infty \tag{4}$$

and the multiplicity of each eigenvalue is finite.

$$\Delta f = -\lambda f. \tag{5}$$

Eq. (5) is the Laplacian eigenvalue problem and it must be noticed that the solutions define the spatial part of solutions of the wave equation. Solving Eq. (5) on each hippocampus triangulated surface as a Riemannian manifold gives us corresponding eigenvalues and eigenfunctions. For the numerical computations, the software (ShapeDNA-tria) provided by Martin Reuter was used for cubic FE method approximations as first proposed in [9].

The global investigation is performed only over the first 20 eigenvalues based on the results of [10]. The addressed study shows that using too many eigenvalues has an undesirable effect on the statistical significance. The mentioned effect occurs due to the fact that higher order eigenvalues correspond to higher frequencies which are more likely to be noisy. Also, it is shown in [10] that Laplace Beltrami spectrum is capable of representing shape differences while size differences are removed by surface area or volumetric normalization. Our data is normalized to unit surface area for global analysis.

The local investigation is performed over the second non-constant eigenfunction. Since higher order eigenfunctions correspond to higher frequencies, lower order eigenfunctions are more robust against noise. It can be seen in Fig. 2 that second eigenfunction gives us simple localized geometric features. Topological methods including construction of the MS complex and finding the zero level set are performed for computing presented local shape descriptors. These methods simplify the high dimensional eigenvectors which are proportional to the total number of vertices on triangular meshes of each hippocampus.

2.2. The topological methods

Morse Theory can be utilized for topological analysis of eigenfunctions. Critical points, where the gradient vanishes, play an essential role in Morse theory. If the Hessian at a critical point is non-singular, that point is non-degenerate. If all of the critical points of a function are non-degenerate, then it is called Morse function. In a Morse function, MS complex could be obtained by finding integral line of gradient vector field from the saddles to the minima and

maxima. These integral lines, which are edges when MS complex represented as a graph, connect saddles, minima, and maxima that are nodes of this graph [11].

In this paper MS graphs are used for local topological analysis of Hippocampus. In the first stage the critical points are computed. The critical points are assumed to be at vertices. The minimum is a vertex whose Morse function value is less than the values of all its neighboring vertices while the maximum is a vertex with a higher value than its neighbors. In saddle point the difference between its value and its neighbors, switches the sign four or for more than four times while this difference switches the sign twice in the case of regular points.

The second stage for obtaining MS graph is going along the gradient field, from each saddle up to the maxima and down to the minima of Morse function. If we have more than one option, the steepest slope should be followed. Figure 2 indicates the MS complex of the second eigenfunctions of a normal hippocampus (For more details see [12]).

In addition to MS complex we used the zero level set of the eigenfunction as a local shape descriptor. As Reuter did in [10], finding zero level set curves starts at the intersection of an edge and zero level set line of the eigenfunction. The procedure continues by searching through the surface and finding other intersections on the neighboring triangles until the starting edge is reached.

2.3. Feature extraction

Proposed sets of features for each subject measure the dissimilarity between left and right hippocampus size descriptors, global shape descriptors and, local shape descriptors. The first set of features which are based on volume and surface area measurements are used to investigate the size differences between the right and the left hippocampus. Eq. 7 calculates the surface area differences (SD) using the right and the left hippocampi surface areas (R_{sa} and L_{sa}) as follows:

$$SD = \frac{L_{sa} - R_{sa}}{L_{sa} + R_{sa}}. \quad (7)$$

The volume differences (VD) were computed through the same method. In this case the volume of each hippocampus is calculated as the number of voxels inside the 3D hippocampus, multiplied by the spatial volume occupied by each voxel. The hippocampus surface area is estimated by adding the areas of triangles constructing the hippocampus triangulated surface.

The second set of features includes global shape descriptors dissimilarity (GSD). These features which use the first 20 eigenvalues are defined as the ratios of right to left hippocampus eigenvalues.

The third set of features uses Laplace Beltrami eigenfunctions. These functions are studied with topological methods. The MS complex and zero level sets construct almost the same curves on each hippocampus due to the similar geometries of hippocampi and eigenfunctions corresponded to these intrinsic geometries. These curves are illustrated in Fig. 2. The MS complex paths presented with black and red colors identify the length of upper part and lower part of hippocampus (LU and LL), in addition to the length of hippocampus (L) and the waist circumference (WC). Zero level sets depicted with green curves identify the head circumference (HC) and tail circumference (TC) according to their position around the hippocampus. These local shape descriptors form our third set of features by computing their differences of each person's right and left hippocampus, yielding {LD, LUD, LLD, WCD, HCD, TCD}.

Having these three sets of features can result in a feature vector which is computed for each subject and is utilized in next stage.

2.4. Classification

In classification step, first all subjects are classified to epileptic patients and normal subjects using the classifier 1, then epileptic patients are labelled as patients with RTLE or patients with LTLE by means of the classifier 2. In both cases the Support Vector Machine (SVM), a powerful classification tool in medical applications, is applied.

Feature selection method is utilized in order to reduce the dimension of the proposed feature vector to choose the best set of features for each classifier. The subset selection algorithm is used to search through the space of possible subsets with one, two or three features and evaluate each subset by running the classifier on it. Although the method is computationally expensive in training stage, it guarantees the best subset.

3. RESULTS

Our dataset consists of 71 T1-weighted MR images, acquired at Henry Ford Hospital (HFH), Detroit, MI, USA, containing 12 normal subjects in addition to 28 epileptic patients with RTLE and 31 epileptic patients with LTLE. The subjects' slices are 256×256; voxel sizes are $0.78 \times 0.78 \times 2$ mm^3 (Slice thickness: 2 mm).

The HFH data contains manually segmented hippocampi. We obtained 3D binary shapes and extracted triangulated surfaces and used them in size measures and computing local shape descriptors. Our data is also normalized to unit surface area and employed to calculate global shape descriptors. Consequently 28 features are computed for each subject in feature extraction steps. The next task is to reduce the size of the feature vector using subset selection algorithm and input it into the classification stage.

Two stages of classification are performed to differentiate between NS and EP, and patients with RTLE and patients with LTLE. SVM classifier is used in each stage. For both classifiers a Gaussian kernel is hired; meaning that our input feature space is mapped to an infinite dimensional space. Selected set of features for each classifier is presented in Table 1.

In both classifiers the accuracy of classification is computed in a leave-one-out cross-validation as the percentage of correct classifications. Since the number of our normal subjects is not proportional to the number of epileptic patients, we also calculated the sensitivity and specificity of classifier 1 for epileptic diagnosis. These results are presented in Table 2 and 3 together with volumetric analysis by using just the volume based feature

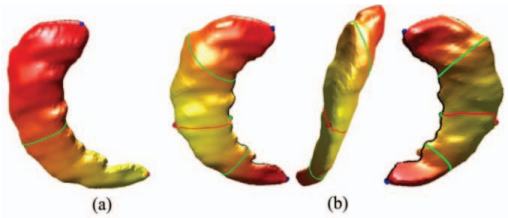


Fig. 2: A sample normal hippocampus covered with color shades which depict first and second non-constant eigenfunctions in (a) and (b) respectively. Maxima and minima are presented with blue and red dots and saddles with green ones. Closed green curves highlight the zero lets of the proportional eigenfunctions and integral lines with red and black curves show MS complex paths.

and shape analysis based on spherical harmonics. Table 2 presents the quantified performance of the proposed method in epilepsy diagnosis. It also depicts an improvement over volumetric analysis.

Table 1: the best set of features chosen by subset selection algorithm for each classifier.

	Selected set of features
Classifier 1	SD, GSD_{15}, GSD_{18}
Classifier 2	TCD, GSD_{11}, GSD_{15}

Table 2: Epileptic patient and normal subject results comparison using proposed method and volumetric analysis.

Classification	Proposed method	Volumetric analysis
Sensitivity	94.9%	88.1%
Specificity	83.3%	50.0%
Accuracy	93.0%	81.7%

Table 3 shows the epilepsy lateralization results of the proposed method and its comparison with volumetric analysis and spherical harmonics method presented in our previous work [5].

Table 3: Comparison of the epilepsy lateralization results of the proposed method, volumetric analysis and spherical harmonics.

Classification	Accuracy
Proposed method	86.4%
Spherical harmonics	84.7%
Volumetric analysis	78.0%

Relative to the previous studies [5-8], like utilizing spherical harmonics, our method has generated comparable accuracy. The results show significant improvement over using the volumetric features alone. In [6], the best results of 96.3% accuracy for epilepsy diagnosis and 90.3% for lateralization are reported which are superior to our results but their dataset includes just epileptic patients with anterior temporal lobe focus which is more specific than our data of patients with different types of TLE.

4. CONCLUSION

This paper presents an alternative methodology to identify epileptic patients and distinguish between RTLE and LTLE, based on local and global shape analysis of hippocampus. The proposed method is isometric invariant, hence in contrast to other methods there is no needs for registration and alignment. Utilizing lower order eigenvalues and eigenfunctions corresponding to lower frequencies gives robust shape descriptors with respect to noise and shape change. The classification results show that proposed shape features are useful for diagnosis of epilepsy and lateralization purposes.

Future work will focus on finding more level sets around the hippocampus triangulated surface for more localized shape analysis. Moreover it is interesting to compute the global features regionally using the local features. In this case the hippocampus could be divided into specific regions indicated by local geometries.

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