Lateral ventricle morphology analysis via mean latitude axis

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Abstract:

Statistical shape analysis has emerged as an insightful method for evaluating brain structures in neuroimaging studies, however most shape frameworks are surface based and thus directly depend on the quality of surface alignment. In contrast, medial descriptions employ thickness information as alignment-independent shape metric. We propose a joint framework that computes local medial thickness information via a mean latitude axis from the well-known spherical harmonic (SPHARM-PDM) shape framework. In this work, we applied SPHARM derived medial representations to the morphological analysis of lateral ventricles in neonates. Mild ventriculomegaly (MVM) subjects are compared to healthy controls to highlight the potential of the methodology. Lateral ventricles were obtained from MRI scans of neonates (9-144 days of age) from 30 MVM subjects as well as age- and sex-matched normal controls (60 total). SPHARM-PDM shape analysis was extended to compute a mean latitude axis directly from the spherical parameterization. Local thickness and area was straightforwardly determined. MVM and healthy controls were compared using local MANOVA and compared with the traditional SPHARM-PDM analysis. Both surface and mean latitude axis findings differentiate successfully MVM and healthy LV morphology. LV in MVM neonates show enlarged shapes in tail and head. Mean latitude axis is able to find significant differences all along the LV shape, demonstrating that local thickness analysis provides significant insight over traditional SPHARM-PDM. This study is the first to precisely quantify 3D lateral ventricle morphology in MVM neonates using shape analysis.

Purpose:

Quantitative morphologic assessment of individual brain structures is often based on volumetric measurements. Volume changes can intuitively explain atrophy or dilation due to illness but changes at specific locations are not sufficiently reflected in global volume measurements. Statistical shape analysis has emerged as a way of evaluating location and magnitude of morphology in brain structures. Since shape frameworks are surface based and directly depend on the quality of surface alignment, current shape methodologies are not able to differentiate shape changes from positional differences [1]. In contrast, medial axis descriptions employ thickness information as alignment-independent shape metric. Medial algorithm development started few decades ago [2] as a way to extract medial representations (m-rep) from object boundaries. Since then, medial model methodology is a widely used technology for solving problems of the medical image analysis community [3], such as segmentation or shape analysis [4][5].

We propose a quasi-medial representation model to independently analyze volume and positioning that inherits the shape-constrained point correspondence of the well-known spherical harmonic (SPHARM-PDM) shape framework. One of the main advantages of the proposed framework is that it is and end-to-end free open source software (FOSS) solution, as part of Slicer [6]. The SPHARM-PDM toolbox module in Slicer intends to bridge the gaps between the experimental science made by computer scientists and the clinical research science, making it available to a bigger audience that does not need to have a big computer expertise or deep understanding of the underlying basic science to operate the tool.

We validated our integrated shape and mean latitude axis analysis framework by assessing the pathological variations of the pediatric lateral ventricles (see figure 1) by applying our method to a large database of neonatal scans. This database included a cohort of Mild ventriculomegaly (MVM) subjects that we decided to compare to healthy controls in order to highlight the potential of the methodology. MVM is characterized as the prenatal enlargement of the cerebral lateral ventricles and identified by ultrasound measurement of the atrial width of the fetal lateral ventricle in-utero [7]. The cause of MVM is unknown, and to date there are no studies that analyze MVM morphology compared to healthy morphology. Enlargement of the cerebral lateral ventricle has been observed in many psychiatric disorders, including schizophrenia, and has been recognized as a potential biomarker for identifying early abnormal brain development [8].

Data:

Ninety pairs of lateral ventricles were used for this study, 30 MVM and 60 age- and sex-matched control obtained from MRi scans. Images were acquired on a Siemens 3T scanner (Allegra, Siemens Medical System, Erlangen, Germany). Infants were scanned unsedated while asleep, fitted with ear protection and had their heads secured in a vacuum fixation device at both 1 and 2 year follow up sessions. T1-weighted, proton density and T2-weighted images were obtained. Spatial resolution was 1x1x1 mm for T1-weighted images, 1.25x1.25x1.5 mm with .5 mm gap for PD/T2-weight images.

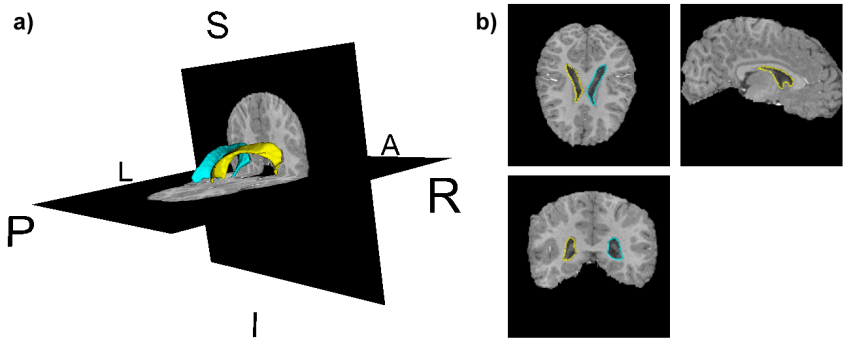

Figure 1 Pediatric LV segmented in a 2-year-old MRI scan. a) 3D rendering of the right (yellow) and left (cyan) lateral ventricles displayed in coronal and axial cross-sections of the brain for anatomical reference b) Axial (top-left), sagittal (top-right) and coronal (bottom-left) cross-sections of the brain with LV slice intersections visible.

For all datasets, the LV segmentation was performed manually, i.e., outlining the LV visible in the cross-sections of the MRi scans, via InsightSNAP [9]. Correspondence of SPHARM-PDM point-based correspondent models computed from LV segmentations were quality controled. From the 90 initial pairs of LV, 78 lefts (26 MVM and 52 sex- and age-matched controls) and 75 right (25 MVM and 50 sex- and age-matched controls) lateral ventricles were selected for the study.

Method(s):

In summary, the spherical harmonic (SPHARM) shape description is a hierarchical, global, multi-scale boundary description that can represent objects of spherical topology, proposed initially by Brechbuhler et al. [10] This shape framework is based in spherical parameterization that is computed via optimizing an equal area mapping of the 3D voxel mesh onto the sphere and minimizing angular distortions. The basis functions of the parameterized surface are spherical harmonics. Each individual SPHARM description is composed of a set of coefficients, weighting the basis functions. Based on a uniform icosahedron-subdivision of the spherical parameterization, we obtain a Point Distribution Model (SPHARM-PDM) [11].

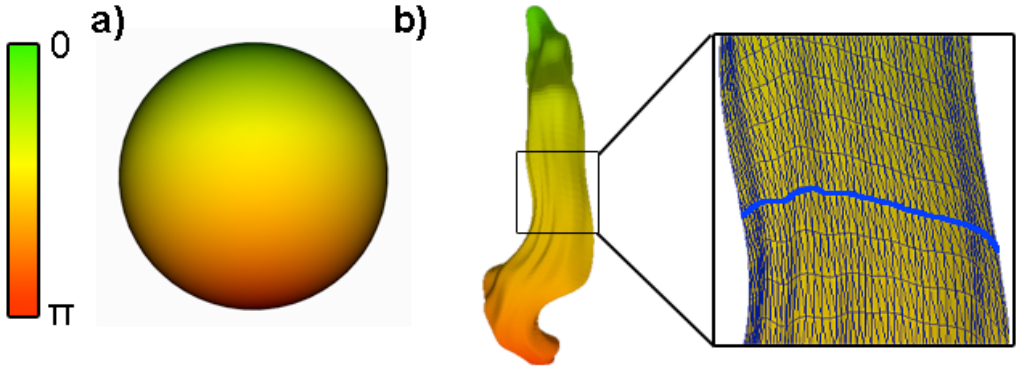

Figure 2. a) Theta parametric field where north pole = 0 and south pole = π. b) Superior view of the SPHARM medial mesh of a left LV. The close up shows the iso-latitude lines (one of the lines, highlighted bold blue line).

We propose a quasi-medial representation model to analyze independently volume and positioning that inherits the shape-constrained point correspondences from SPHARM-PDM computed models. Mean latitude axis is not a full medial representation but its computation is straightforward and easily to compute from the boundary descriptions already provided by SPHARM-PDM. This idea was initially proposed by Kim et al. [1], however our proposal differs in the way the mean medial axis is computed (see figure 2): after calculating a parameterization of all points of the initial 3D voxel mesh, a medial mesh is computed by dividing the theta (θ) parametric field with values between [0, π] a fixed number of times specified by the user (in SPHARM-PDM, this parameter is called theta_iterations). A theta_iterations number of iso-latitude lines will then placed at equally valued latitudes in the new SPHARM Mesh. A number of points also specified by the user (in SPHARM-PDM, this parameter is called phi_iterations) will be then placed along each iso-latitude lines. The new medial mesh will have then theta_iterations x phi_iterations number of vertices. The 3D locations of the mean latitude axis will be then calculated by averaging all points along each iso-latitude line. The number of points of the medial mesh will be theta_iterations.

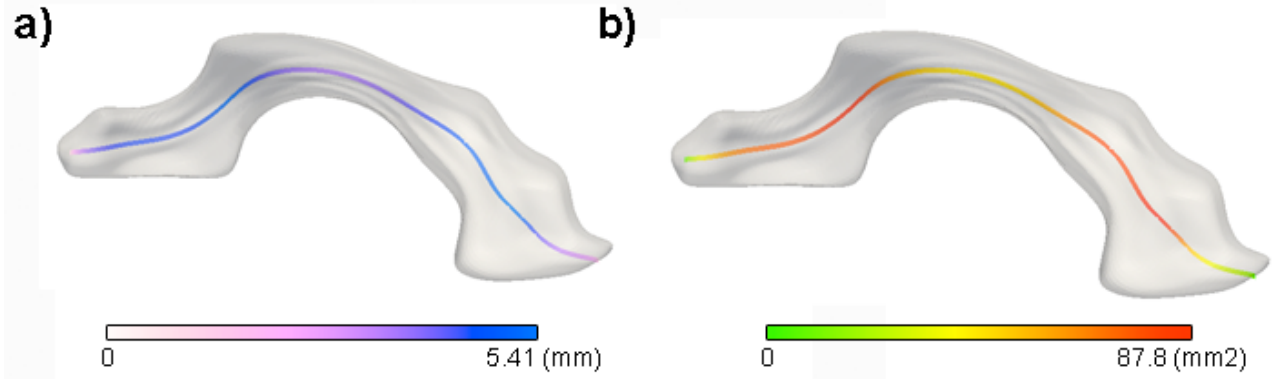

Figure 3. Mean latitude axis metrics, sagittal view of an example neonatal LV a) Radius b) Area.

Both surface and mean latitude axis descriptors will be used to analyze LV morphology, and differentiate between MVM and healthy subjects at neonatal stage in a cross-sectional groupwise study.

- Surface metrics: The point-based models will be analyzed using multivariate analysis of covariance (MANCOVA) [12]. Age and gender will be used as covariants. Point-wise p-value maps of group differences displayed over the whole surface will be provided as results.
- Mean latitude axis metrics: Two alignment-independent metrics calculated from mean latitude axis are proposed. Mean radius across each iso-latitude line (figure 3.a.), and area of each iso-latitude cross-section (figure 3.b.). Point-wise p-value for the difference in group least-squares means displayed over the mean latitude axis will be provided as results for both radius and area.

Results:

Shape results (figure 4) are presented via color coded p-values maps, visualized over a mean LV surface. In the map, highly significant correlations ($p < 0.001$) are color-coded with red and green ($0.01 > p > 0.05$) and non-significant correlations are color-coded with blue. The main areas of significance in our comparison analysis for the left LV are primarily located on the lateral aspects of the anterior and posterior sections. The right LV exhibits fewer clusters of significance than seen in the left, but significance is also primarily located in the posterior and anterior aspects of the main body of the ventricle. This suggests that the enlargements seen in our MVM cohort tend to occur in the anterior and posterior sections of the LV more often than in the medial sections. Mean latitude axis results are presented via color coded p-values maps, visualized over the mean latitude axis of a LV that is used as template. Mean latitude axis disentangles shape and position, and therefore both area and radius are able to differentiate successfully LV morphology between MVM and healthy age- and sex-matched controls. Mean latitude axis, therefore, is an excellent method to detect abnormal LV morphology in neonates.

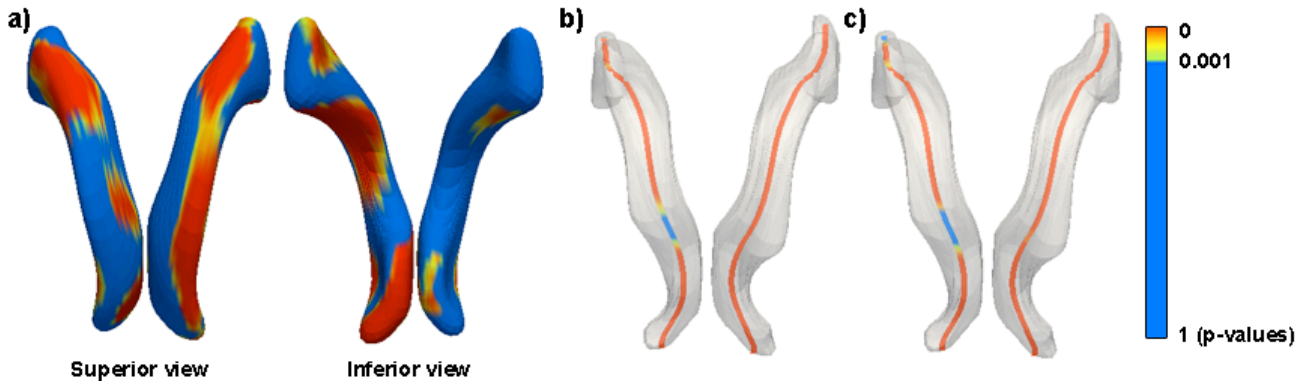

Figure 4. P-values of a) surface and b) axis differences between MVM and healthy control cross-sectional group analysis displayed over a) mean LV surfaces (superior and inferior views) and b) template ventricle mean latitude axis.

Conclusions:

By using inherent correspondences of SPHARM-PDM, mean latitude axis allowed shape-constrained correspondence without a registration step. Disentangling shape from positioning anomalies may provide new insights in the pathogenesis of a variety of other brain disorders in which these morphometric characteristics coexist. We previously quantified local volume changes to differentiate MVM and healthy controls in neonatal age [13]. To date, this is the first study that has analyzed shape morphology in an MVM cohort. We have successfully identified that the regions of enlargement are primarily located in the anterior and posterior sections of the lateral ventricle. Interestingly, in a recent study analyzing longitudinal shape morphology changes in healthy individuals, we also found that the anterior and posterior regions of the lateral ventricle experienced the highest growth rates in the first two postnatal years [14]. This suggests that it is possible enlargement of the cerebral lateral ventricles in MVM could be a result of potential accelerated expansion of these dynamic areas during the prenatal stages of development. We have shown here that assessing LV morphology at the early stages of brain development provides useful information for locating and quantifying shape changes between MVM subjects and sex- and age-matched controls. Mean latitude axis successfully differentiates abnormal LV morphology of MVM in neonates and provides a more detailed picture of the structural changes that lead to pathogenesis in MVM.

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