Automated Segmentation of Ventricles from Serial Brain MRI for the Quantification of Volumetric Changes Associated with Communicating Hydrocephalus in Patients with Brain Tumor

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ABSTRACT

Accurate ventricle volume estimates could improve the understanding and diagnosis of postoperative communicating hydrocephalus. For this category of patients, associated changes in ventricle volume can be difficult to identify, particularly over short time intervals. We present an automated segmentation algorithm that evaluates ventricle size from serial brain MRI examination. The technique combines serial T1-weighted images to increase SNR and segments the means image to generate a ventricle template. After pre-processing, the segmentation is initiated by a fuzzy c-means clustering algorithm to find the seeds used in a combination of fast marching methods and geodesic active contours. Finally, the ventricle template is propagated onto the serial data via non-linear registration. Serial volume estimates were obtained in an automated robust and accurate manner from difficult data.

Keywords: Brain imaging, MRI, brain tumor, communicating hydrocephalus, segmentation, monitoring.

1. INTRODUCTION

Changes in lateral ventricle size and structure are often observed in association with neuropathologies, such as brain tumors [15,16]. High resolution, serial MR imaging facilitates non-invasive monitoring and evaluation of the tumor size in patients with brain lesions. Furthermore, routine clinical observation of such studies suggests that that ventricle size progressively increases in many of these patients. This likely represents a communicating hydrocephalus [4], a phenomenon with still unclear etiology. In these patients, blood and proteins introduced into the cerebrospinal fluid (CSF) during surgical resection may lead to chronic dilation of the lateral ventricles.

Ventricular size changes are subtle, even by comparison of coregistered images. Nevertheless volumetric measurements over a period of time may play an important role in identifying the incidence of hydrocephalus, and to correlate the presence or absence of such a phenomenon with clinical symptoms. Therefore, we sought an objective method to systematically characterize the clinical observation of progressive ventriculomegaly in this group.

In previous work, ventricles were segmented using region-growing combined with anatomical knowledge [12] in images of high quality. Holden et al. [4] used non-rigid registration combined with data from an atlas to segment brain ventricles, relying on the high performance of the registration algorithm. The registration with an atlas is also addressed in [9] using an expectation-maximization joint model. Recently, Hu and Collins [6] proposed a model-based segmentation on multi-modality MR images. A disadvantage of atlas and model-based methods is the large number of training cases needed. In particular, the choice of data used to create the atlas can affect the ability of such methods to address the wide range of topologies in the lateral ventricles.
Many prior studies deal with high resolution data from uniform data sets. Because our data comes from patients with brain tumors on a number of different imaging platforms, image contrast can be quite variable and signal-to-noise ratio (SNR) low. Therefore, our method was designed to exploit patient-specific data for better-adapted intra-patient non-rigid registration, less sensitive to image quality and the anatomical variability of brain tumor patients. Mean T1 images with increased SNR are analyzed and automated seeds are selected throughout the ventricles to avoid excluding the horn and communicating cisterns. Hence, no correction for inhomogeneous signal intensity is required. The seeds provide the input for the fine segmentation based on geodesic active contours. Finally, the mean ventricular shape is adaptively propagated through the temporal data to quantify size changes.

This work proposes an objective method to systematically characterize the clinical observation of progressive ventriculomegaly in this group of patients. Because of the complex alterations of brain morphology in our patients, the segmentation of brain ventricles is challenging. Surgical interventions result in communication between the ventricular system and the cisterns, while the development of tumors contributes to shape alterations. T1 images obtained post contrast add the complication of enhancing tissue (i.e. choroid plexus in the ventricles, and tumors), raising the number of tissue classes in the brain. Edema and gliosis also result in signal intensities overlapping with CSF. These factors complicate the segmentation of ventricles for this class of patients with postoperative communicating hydrocephalus.

2. METHOD

2.1 DATA

Patients with brain tumors evaluated at the Clinical Center of the NIH were scanned on 1.5 T GE (Milwaukee, WI) or 3 T Philips (Best, Netherlands) MR systems at approximately one to three month intervals. As part of the routine clinical imaging, T1 weighted sequences were obtained following injection of an intravenous contrast agent. Images were acquired on sagittal or axial views and reconstructed with approximately 1 mm isotropic voxel size.

Parameters were trained on four patient datasets not included in the validation. For error quantification, manual segmentations of the ventricles were performed at five time points on four patients MRI series (20 scans). An additional 27 serial MRI datasets were automatically segmented and quantified. Patients were imaged with MRI between nine and 33 times at one to three month intervals over a maximum of four years. The total number of time-point scans for the 31 patients was 414. Figure 1 shows six time points from the MRI data of a patient.

![Figure 1: Time points from the MRI data of a patient. The evolution of the lateral ventricles can be observed in chronological order from left to right. Note the changes in intensity, homogeneity and noise between temporal images.](image)

2.2 PREPROCESSING

For each patient, the 3D datasets were coregistered to the first dataset in the series using a six-parameter rigid body transformation (translation + rotation) and a least squares cost function. To normalize the dataset, a large ~100 cc volume of interest (VOI) was automatically placed in the brain volume in relation to its center of mass (Figure 1). The histogram of this VOI was used to identify the modal signal intensity representing white matter. Each dataset was normalized by dividing by this value, and a high signal-to-noise ratio (SNR) “mean” image was generated for each patient by averaging the time point datasets.

Successive pre-processing steps consist of the following steps:
• Extraction of the mid-sagittal plane (MSP) on the original image [5].
• Skull-stripping using a brain extraction tool (BET) [15].
• Smoothing the extracted brain with anisotropic diffusion [8].
• Performing global histogram analysis on the extracted brain and least-squares fitting with separate Gaussian peaks corresponding to the background, CSF, grey matter (GM), and white matter (WM) [17].

2.3 SEED SELECTION FROM FUZZY C-MEANS CLUSTERING

The fuzzy c-means membership (FCM) [1] was computed for the three main classes of brain tissue (grey matter – GM, white matter – WM, and cerebrospinal fluid – CSF) and their intermediates (CSF/GM and GM/WM). \( u_{ij} \) is the degree of membership of \( x_i \) to cluster \( j \) centered on \( c_j \).

\[
J = \sum_i \sum_j u_{ij} \| x_i - c_j \|_2^2
\]

Thresholding was performed on a 0.5 and 0.8 membership value for CSF and CSF/GM, respectively. These values were empirically determined from training cases to adequately include the ventricles and grey intensities in dilated regions. A Euclidean distance filter was used to remove unwanted CSF within the sulci based on the close location to the brain surface. The main body of the lateral ventricles was isolated via morphological operations. This last step provides a rough FCM segmentation for seed placement.

Seeds were found by performing a slice-by-slice analysis downward on the axial view, beginning with the top slice containing the ventricles. The MSP aided in seed placement on the left and right portions of the ventricles. From axial 2D connected components in the search space, blob centroids were designated as seed points. Additional seeds were placed in the axial and coronal slices with the largest CSF component, and the anterior and posterior horns through a caudal-to-rostral search of structures that do not touch the MSP. The latter condition ensures that leakage errors that may be present in the rough FCM segmentation do not provide false positives in the seed selection.

2.4 SEGMENTATION

The second stage of the method is the segmentation of lateral ventricles and our approach uses a combination of fast marching and geodesic active contour level sets [3, 11]. The fast marching method assumes that the surface can only expand staring from the seeds. The speed of expansion is constant and along the surface normal \( n \). The MRI scan \( I \) provides the feature image, while the sigmoid of the gradient of \( I \) supplies the speed function \( I_e \). The first segmentation given by the fast marching level set is \( I_f \).

\[
\frac{dI_f}{dt} + n I_e \nabla I_f = 0
\]

A better-adapted level set based on geodesic active contours in used to refine the fast marching segmentation [3]. To initialize the model, we use the fast marching segmentation as input level image (zero-level) into the geodesic active contour \( I_c \). \( c \) represents the speed and \( k \) the curvature [3].

\[
\frac{dI_c}{dt} = I_c (s + k \| \nabla I_c \|_2 + \nabla I_e \nabla I_c )
\]

2.5 PROPAGATION

Differences in the brain anatomy between serial scans are mainly due to the effects of therapeutic interventions, such as surgery and chemotherapy as well as disease progression (e.g. tumor growth or hydrocephalus). We employ the non-linear registration algorithm based on B-splines [10] to complete the spatial normalization started with the rigid transformation. The registration is performed at three scales from coarse to fine and the number of degrees of freedom is adapted to account for more global or local transforms. The normalized mutual information \( M \) [16] provides the
similarity metric, where $p(I,J)$ is the joint entropy of images $I$ and $J$, and $p(I)$ and $p(J)$ their marginal entropies, computed from the intensity distributions of $I$ and $J$. For more detail on the B-spline definition of the transformation $T$, please refer to [10].

$$M(I | J) = \frac{p(I) + p(J)}{p(I,J)} ;$$

The resulting intra-patient deformation fields between the mean image and the temporary acquisitions are applied to the ventricle template segmented from the mean image using a nearest-neighbor interpolation. Propagated segmentations were validated against manual segmentation at five time points for each test case. As previously noted, patients in our dataset also underwent surgical intervention for the brain tumors. As a result of tumor resection, some shunting between the lateral ventricles and the resected areas occurred. In these cases, the resected regions are also included in the manual and automated results; otherwise, the regions are excluded from the analysis.

3. RESULTS

An example of seed selection to initialize the segmentation of ventricles is shown in Figure 2. At least ten seeds were placed automatically per case and adapted to the morphology of each patient ventricle, as seen by their placement in the horns. The MRI in Figure 2 represents the mean image on which segmentation is performed. This mean image has increased SNR as compared to a single scans (Figure 1). The automated segmentation of ventricles from the mean T1 brain MRI is shown in Figure 3. Comparative results are presented at different stages of the algorithm. In Figure 4, the temporal evolution of ventricular volumes in one patient with communication hydrocephalus is illustrated.

For the quantification of segmentation/propagation results, we compared the data processed by our algorithm with manually-segmented data from 20 MRI scans from four patients (five acquisitions/patient). The mean error in volume estimation was 9±3.8 %. The symmetric overlap was 92.4±1.7 % and root-mean square error 1.3±0.7 mm.

The effects of surgery and treatment on the temporal evolution of the lateral ventricles are shown in Figure 5. Both patients underwent brain resection followed by ventricular shunt placement. Other interventions (e.g. drug therapy) in addition to surgery were probably administered to the patients studied in Figure 5, accounting for the fluctuations in ventricular size.

![Figure 2: Automated seed placement for initializing the ventricle segmentation on the mean image. Seeds (shown by crosses) were placed in the first axial slice with lateral ventricle CSF, in the axial slice containing the largest ventricular area, and in the anterior and posterior horns. Additional seeds are no shown in the picture.](image-url)
4. DISCUSSION

The quantifications of ventricular volumes show great promise for ventricular size change assessment and confirmation of radiological observations related to the possible relation between brain tumor resection and communicating hydrocephalus. Moreover, the technique is fully automated and avoided the inter- and intra-user typically associated with interactive methods [2]. The proposed technique was robust on 31 patient data with 414 time point acquisitions. Quantitative results on test data showed high accuracy on images with low signal-to-noise-ratio (SNR) and morphological abnormalities in the brain.

First, intra-patient data were registered using a rigid transformation and normalized in intensity. A mean image was computed from the normalized temporal scans of each patient, which has increased SNR than temporal scans. Subsequently, the lateral ventricles were segmented from the mean data, using fast marching and geodesic active contour level sets. The level sets were initiated by automatically placed seeds via fuzzy c-means clustering and mid-sagittal plane detection. The mean image was registered to each temporal scan of the same patient by non-linear registration and the ventricle template was propagated through the temporal scans.

Figure 3: Segmentations on the mean image using only adaptive FCM (top) and using level-sets after FCM initialization (bottom). The advantages of using level-sets is shown by the more complete ventricular segmentation, including the extraction of anterior and posterior horns.

Because the segmentation was initially performed on a high SNR dataset created from all component data sets, it is not necessary for the segmentation to be successful on each individual dataset. Therefore, an individual dataset which is noisy or artifact-ridden (e.g. from patient motion) can be evaluated. Moreover, region growing, level sets starting from a single seed and statistical algorithms are affected by contrast enhancement. Using multiple seeds for segmentation at different levels of the ventricles, our technique avoided the obstruction caused by the presence of contrast agents in the choroid plexus and adapts to the morphology of the patient’s ventricle. The use of flexible active contours in our
method handled the varied ventricular structures in our dataset. In comparison, the fuzzy c-means method, an adaptive threshold, was not able to account for partial volume effects and contrast enhancement (Fig. 2), but provided a good initialization for the active contours.

The algorithm will allow the distinction between cases that show an increase in ventricular size and those without hydrocephalus to support the documentation of the tumor related brain atrophy. Future work will include an adaptive determination of edge image parameters in the level-set formulation. Furthermore, improving anatomical knowledge through registration or extraction of cortical landmarks will be explored.

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![Graph of manual (blue squares) versus automated (red dots) ventricular volume estimation.](image)

**Figure 4:** Graph of manual (blue squares) versus automated (red dots) ventricular volume estimation. This example shows the automated quantification of ventricular growth of the patient with brain tumor presented in Figures 1, 2 and 3. The bottom image illustrates 3D renderings of the automated ventricular volumes at the points of comparison with manual segmentation (blue squares). Although the change in ventricles between subsequent scans is not obvious.
Figure 5: Monitoring the lateral ventricle volume changes in patients with brain resection and ventricular shunt placement. The absolute volumetric changes are presented in blue (x) and the relative volumetric changes of the ventricles in green (o). Blue squares mark the time of the resection and red squares the time of the shunt placement.
REFERENCES