Automatic Segmentation of Neonatal Ventricles from Cranial Ultrasound for Prediction of Intraventricular Hemorrhage Outcome

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Abstract— Intraventricular hemorrhage (IVH) followed by post hemorrhagic hydrocephalus (PHH) in premature neonates is one of the recognized reasons of brain injury in newborns. Cranial ultrasound (CUS) is a noninvasive imaging tool that has been used widely to diagnose and monitor neonates with IVH. In our previous work, we showed the potential of quantitative morphological analysis of lateral ventricles from early CUS to predict the PHH outcome in neonates with IVH. In this paper, we first present a new automatic method for ventricle segmentation in 2D CUS images. We detect the brain bounding box and brain mid-line to estimate the anatomical positions of ventricles and correct the brain rotation. The ventricles are segmented using a combination of fuzzy c-means, phase congruency, and active contour algorithms. Finally, we compare this fully automated approach with our previous work for the prediction of the outcome of PHH on a set of 2D CUS images taken from 60 premature neonates with different IVH grades. Experimental results showed that our method could segment ventricles with an average Dice similarity coefficient of 0.8 ± 0.12. In addition, our fully automated method could predict the outcome of PHH based on the extracted ventricle regions with similar accuracy to our previous semi-automated approach (83% vs. 84%, respectively, p-value = 0.8). This method has the potential to standardize the evaluation of CUS images and can be a helpful clinical tool for early monitoring and treatment of IVH and PHH.

I. INTRODUCTION

Premature neonates (born before 30 completed weeks of gestation) are at the highest risk of intraventricular hemorrhage (IVH) [1]. IVH is categorized in four grades (grades 1-4, where 4 is the most critical) based on the severity of bleeding [2]. Delayed detection of IVH followed by post-hemorrhagic hydrocephalus (PHH) can lead to brain damage with adverse neurodevelopmental outcomes [3]. Cranial ultrasound (CUS) is a widely used imaging examination that is simple and safe to diagnose IVH in premature neonates [4]; yet, its evaluation is limited by the subjective evaluation in routine clinical assessments. In our previous work [5], we showed how CUS-based quantitative image analysis of cerebral ventricles in premature neonates with IVH could be helpful to noninvasively and non-subjectively predict the progression to severe PHH and identify neonates who are at risk sooner. In that method, we considered a total of 70 morphological parameters from each ventricle, which were segmented manually in 2D CUS images. However, manual segmentation is dependent on user knowledge and reduces the reproducibility of the method.

Although a number of automatic or semi-automated ventricle segmentation approaches have been proposed for computed tomography [6] and magnetic resonance images [7], most of them considered healthy or adult populations. Moreover, only a few US-based segmentation methods have been presented for neonates with IVH [8]-[10]. Ventricle segmentation in US images, especially for premature neonates, is challenging due to different shape, size, and texture characteristics [9]-[11]. In [8], Sciolla et al. proposed a semi-automatic method to segment ventricles in 3DUS images. They computed a feature map using a phase asymmetry criterion and employed an active contour model initialized manually by three seeds to localize ventricles. In [9], Qiu et al. presented a semi-automatic ventricle segmentation method for 3DUS images using convex optimization. Later, they developed an automatic method for neonatal data with different IVH grades [10]. In this latter method, they extracted each ventricle region using the combination of phase congruency map, multi-atlas initialization technique, atlas selection strategy, and a multiphase shape-driven geodesic level-set. Although 3DUS imaging is optimal for monitoring the ventricle volume, current clinical diagnosis is often made based on 2DUS images of brain due to cost and availability. Thus, an accurate segmentation method for 2DUS images is a much needed tool within the routine clinical environment. In [12], Battikha et al. proposed an automatic method for ventricle segmentation in 2DUS images using the combination of a sparse gradient counting method, a simple linear iterative clustering method, and random walker algorithm. In spite of the promising results reported, further validation with neonates with IVH is required.

In this paper, we first present a new fully automatic ventricle segmentation method for 2D CUS images acquired from neonates with IVH. Then, we predict the outcome of PHH and necessity of intervention using the morphological features extracted from lateral ventricles, building on our previous semi-automatic method in [5].
II. MATERIALS AND METHODS

In this study, we considered a retrospective dataset (IRB approved) of 60 premature neonates (mean age of 25±9 days) with the following inclusion criteria: (1) less than 29 weeks gestational age, (2) less than 1,500 grams birth weight, (3) survived until discharge from our neonatal intensive care unit, and (4) with different grades of IVH (#grade 1: 12, #grade 2: 20, #grade 3: 9, and #grade 4: 19). Exclusion criteria were the following: (1) congenital brain malformation, and (2) significant subdural hemorrhage on CUS or skull fractures. Overall, 25% (15/60) of infants with IVH received at least one temporizing intervention to treat PHH. For each case, CUS scans were performed using a GE LOGIQ E9 (GE Healthcare Ultrasound, Waukesha, Wisconsin, USA) medical ultrasound system, and interpreted by a pediatric radiologist. From each CUS scan, we selected a slice in the coronal plane at the level of the foramen of Monro for evaluation. In the selected slice, we segmented ventricles automatically using our new method. Then, we extracted the morphological features from each ventricle to predict the necessity of intervention [5].

A. Ventricle Extraction

To extract the brain ventricles, we first obtain the brain bounding box and brain mid-line. These features allow us to automatically estimate the anatomical position of each ventricle and correct for rotation in the image, which is in a small range (≤ 10°). Then, we employ active contours to segment the ventricles. In Figure 1, an overview of our ventricle extraction method is illustrated, which could be an alternative to a state-of-the-art convolutional neural network due to the limited number of datasets.

Step 1: Brain bounding box detection: To detect the brain bounding box, we use the fuzzy c-means algorithm [13]. We set the number of clusters to 3 to define regions in the CUS image with high, medium, and low intensity values. Then, we fit a bounding box to the extracted cluster with a high intensity value, which corresponds to the bone regions, as shown in Figure 1.

Step 2: Brain mid-line extraction: Brain mid-line localization is important for rotation correction, assessment of symmetry, and estimation of the anatomical positions of ventricles. To detect the brain mid-line inside the upper half of brain bounding box, we use the combination of a template matching method [14] and adaptive thresholding [15]. In the template matching method, we first define brain mid-line templates for each data based on training datasets using the leave-one-out approach. Then, we detect the regions with high match probability values. After that, in the detected regions, we apply adaptive thresholding followed by thinning morphological operation to extract the brain mid-line. Finally, we correct the image rotation using the brain mid-line as vertical axis. Figure 1 shows samples of template matching and adaptive thresholding results.

Step 3: Ventricle initialization: Ventricles with hemorrhage are very hypoechoic in US images [16]. Thus, we first estimate the anatomical positions of ventricles in the upper half of the brain bounding box around the extracted mid-line, which utilized 50% of the brain bounding box’s width. The considered search region around the midline is determined empirically. Then, we identify ventricles using the two clusters with the medium and low intensity values obtained in the Brain bounding box detection step (Figure 1). To remove false-positives, we employ the support vector machine (SVM) classifier. We train the SVM using the size, geometry, and curvature descriptors of ventricles, based on our previous work [5]. At the end, we keep two regions with the highest SVM scores on each side of brain mid-line as the initial regions of ventricles. If only one region is detected because of shading, bleeding, or noise in the image, we use the symmetric counterpart around the brain mid-line for the other lateral ventricle.

![Figure 1. Overview of the proposed framework for ventricle extraction using 2D cranial ultrasound (CUS) images including brain bounding box detection, brain mid-line extraction, ventricle initialization, and ventricle segmentation.](image-url)
Step 4: Ventricle segmentation: To segment the ventricles, we employ the region-based active contour [17] initialized automatically using the previous step. To increase the accuracy of the active contour, especially in the areas with low contrast and shading, we use the combination of the obtained cluster in Step 1 with a high intensity value and the phase congruency map [10, 18] instead of original ultrasound intensity values (Figure 1). The phase congruency map detects step-edges in images well and outperforms the gradient based edge detectors in terms of accuracy [10]. In the phase congruency map, we use convex hull for each connected component to fill gaps and increase the accuracy level of active contour. The employed active contour with the phase congruency map is defined in Eqs. (1)-(5).

\[
\frac{\partial \phi}{\partial t}(x) = \delta(\phi(x)) \int_{\Omega} B(x, y) \nabla \phi(y) F(P(y), \phi(y)) \, dy + \lambda \delta(\phi(x)) \nabla \frac{\nabla \phi(x)}{\|\nabla \phi(x)\|}
\]

\[
\delta(\phi(x)) = \begin{cases} 
1, & \phi(x) = 0, \\
0, & |\phi(x)| < \epsilon, \\
\frac{1}{2\epsilon} \left( 1 + \cos \left( \frac{\pi \phi(x)}{\epsilon} \right) \right), & \text{otherwise}
\end{cases}
\]

\[
B(x, y) = \begin{cases} 
1, & |x - y| < r, \\
0, & \text{otherwise}
\end{cases}
\]

\[
P(y) = \sum_{n} \left( \frac{|o_n(y)| - |e_n(y)| - T}{\sqrt{o_n(y)^2 + e_n(y)^2 + \epsilon}} \right)
\]

\[
T = \exp \left( \text{mean} \left( \log(\sqrt{o_n(y)^2 + e_n(y)^2}) \right) \right)
\]

where \( x \) and \( y \) represent coordinates of a pixel in region \( \Omega \). \( \delta(\phi(x)) \) is a smoothed version of the Dirac delta function. \( B(x, y) \) masks local region within a disk of radius \( r \) centered at \( x \). \( \lambda \) is a weight parameter to keep the curve smooth. \( P(y) \) is the phase congruency map with the small value of \( \epsilon \) for numerical stability. \( o_n(y) \) and \( e_n(y) \) are the even and odd quadrature filter responses at scale \( n \). \( T \) is a threshold to remove weak edges. In this research, we set parameters \( \lambda \) and \( r \) to 0.003 and 5, respectively. In addition, we consider a maximum of fifty iterations for the evolving active contour. Further details regarding the method can be found in [10, 18].

B. Prediction of outcome

In this subsection, we aim to differentiate 15 cases that needed intervention from the 45 non-interventional cases, similar to our proposed method in [5]. To do that, we automatically extract 70 morphological features from each segmented lateral ventricle. These features describe the size, geometry, and curvature of each ventricle and find dissimilarity between the left and right lateral ventricles. We rank these features based on their relevance using the SVM classifier. To estimate the performance of the classifier, we employ a 15-fold cross-validation method by doing 256 iterations. In each iteration, we train the classifier using 14 interventional cases and 14 randomly selected non-interventional cases. The remaining one interventional and 31 non-interventional cases are used for validation.

After cross-validation, we select 6 most relevant features (shown in Table I) for the prediction of outcome. The combination of these features provides the maximum sensitivity (100%) for the identification of neonates who are at high risk and require future intervention for their PHH.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Explanation</th>
</tr>
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<tbody>
<tr>
<td>P1</td>
<td>Maximum width of ventricles in mm</td>
</tr>
<tr>
<td>P2</td>
<td>Maximum length of ventricles’ circumscribed ellipses*</td>
</tr>
<tr>
<td>P3</td>
<td>Minimum area of the ventricles**</td>
</tr>
<tr>
<td>P4</td>
<td>Maximum medial length of ventricles***</td>
</tr>
<tr>
<td>P5</td>
<td>Ratio of left to right ventricle medial length</td>
</tr>
<tr>
<td>P6</td>
<td>Ratio of left to right entropies of ventricle thickness</td>
</tr>
</tbody>
</table>

*Normalized by brain diameter; **Normalized by ventricle’s circumscribed ellipse area; ***Normalized by ventricle’s circumscribed ellipse length

III. RESULTS

To evaluate the performance of our segmentation method, we compared the ventricle segmentation results against the ground truth using the Dice similarity coefficient. Ground truth was obtained by manual segmentation under the supervision of an expert neurologist. In Table II, we report the summary of quantitative results (mean, standard deviation-SD, and median) based on the initial and segmented ventricle regions (output results of Step 3 and Step 4) for each IVH group and all cases. In Figure 2, we show three examples, including a challenging case, of the segmented ventricles with their Dice similarity coefficient and IVH grade, which are compared with the ground truth.

The six features presented in Table I were selected to identify the neonates at risk. We predicted the necessity of intervention with accuracy, sensitivity and specificity of 0.83, 1, and 0.65, respectively. These results are similar to those that we reported in the past (accuracy of 0.84, p-value=0.8), but which required manual segmentation of the ventricles for analysis. The prediction based on manual measurement currently used in clinics was previously reported to be 0.76, which was significantly worse (p<0.01) than our reported results. Significance (p-value) was assessed using the Wilcoxon signed-rank test.

IV. DISCUSSION

Ventricle segmentation in US images is difficult, especially for IVH neonates with different shape, size, and texture characteristics. To the best of our knowledge, only a few studies have focused on US-based ventricle segmentation in premature neonates with IVH [8]-[10]. We chose to work with 2D US images, which are often used for clinical diagnostics. Unlike previous methods, we used location and shape information in the initialization of our technique, but not in the segmentation procedure due to the high variability in the shape and position of ventricles with IVH in 2D US images. Figure 2b shows examples of cases with severe IVH that distorts the shape of the ventricles and changes the intensity and texture in the image. For these reasons, our segmentation was guided by a phase-congruency map of edges instead of image intensity.

Experimental results showed that our method could segment ventricles in pathological cases with IVH with an average Dice similarity coefficient of 0.8, compared to the reported 0.77 in [10]. The method also demonstrated robustness in US images with incomplete boundaries because
of shading (an example is shown in Figure 2.a). However, one limitation of the current approach is that its accuracy level is affected by the unclear boundary of ventricles due to the build-up of bleeding pressure. It is important to mention that this is a limitation also in the manual segmentation performed by experts. In addition, our method could predict the necessity of intervention with an average accuracy level of 0.83, which significantly outperforms over the clinical manual measurements [5].

<table>
<thead>
<tr>
<th>Dice similarity for the initial ventricles (Step 3)</th>
<th>Dice similarity for the segmented ventricles (Step 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>Median</td>
</tr>
<tr>
<td>Grade 1</td>
<td>0.69 ± 0.18</td>
</tr>
<tr>
<td>Grade 2</td>
<td>0.73 ± 0.12</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0.81 ± 0.12</td>
</tr>
<tr>
<td>Grade 4</td>
<td>0.77 ± 0.14</td>
</tr>
<tr>
<td>All cases</td>
<td>0.74 ± 0.14</td>
</tr>
</tbody>
</table>

We presented a new CUS-based ventricle segmentation method for premature neonates with IVH and predicted the necessity of intervention automatically. In our segmentation method, we first extracted the brain bounding box and midline to correct the brain rotation and determine the anatomical positions of ventricles. Then, we initialized each ventricle using fuzzy c-means clustering and the SVM classifier. Finally, we completed the ventricle segmentation procedure using the automatically localized active contour and the phase congruency map.

**REFERENCES**


**Figure 2.** Three examples of automatic ventricle segmentation (blue color) against the ground truth (red color) with their Dice similarity coefficient and IVH grade.

**V. CONCLUSION**

We presented a new CUS-based ventricle segmentation method for premature neonates with IVH and predicted the necessity of intervention automatically. In our segmentation method, we first extracted the brain bounding box and midline to correct the brain rotation and determine the anatomical positions of ventricles. Then, we initialized each ventricle using fuzzy c-means clustering and the SVM classifier. Finally, we completed the ventricle segmentation procedure using the automatically localized active contour and the phase congruency map.