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● *Original Contribution*

USER-GUIDED SEGMENTATION OF PRETERM NEONATE VENTRICULAR SYSTEM FROM 3-D ULTRASOUND IMAGES USING CONVEX OPTIMIZATION

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Abstract—A three-dimensional (3-D) ultrasound (US) system has been developed to monitor the intracranial ventricular system of preterm neonates with intraventricular hemorrhage (IVH) and the resultant dilation of the ventricles (ventriculomegaly). To measure ventricular volume from 3-D US images, a semi-automatic convex optimization-based approach is proposed for segmentation of the cerebral ventricular system in preterm neonates with IVH from 3-D US images. The proposed semi-automatic segmentation method makes use of the convex optimization technique supervised by user-initialized information. Experiments using 58 patient 3-D US images reveal that our proposed approach yielded a mean Dice similarity coefficient of 78.2% compared with the surfaces that were manually contoured, suggesting good agreement between these two segmentations. Additional metrics, the mean absolute distance of 0.65 mm and the maximum absolute distance of 3.2 mm, indicated small distance errors for a voxel spacing of $0.22 \times 0.22 \times 0.22$ mm^3. The Pearson correlation coefficient ($r = 0.97, p < 0.001$) indicated a significant correlation of algorithm-generated ventricular system volume (VSV) with the manually generated VSV. The calculated minimal detectable difference in ventricular volume change indicated that the proposed segmentation approach with 3-D US images is capable of detecting a VSV difference of 6.5 cm^3 with 95% confidence, suggesting that this approach might be used for monitoring IVH patients' ventricular changes using 3-D US imaging. The mean segmentation times of the graphics processing unit (GPU)- and central processing unit-implemented algorithms were 50 ± 2 and 205 ± 5 s for one 3-D US image, respectively, in addition to 120 ± 10 s for initialization, less than the approximately 35 min required by manual segmentation. In addition, repeatability experiments indicated that the intra-observer variability ranges from 6.5% to 7.5%, and the inter-observer variability is 8.5% in terms of the coefficient of variation of the Dice similarity coefficient. The intra-class correlation coefficient for ventricular system volume measurements for each independent observer ranged from 0.988 to 0.996 and was 0.945 for three different observers. The coefficient of variation and intra-class correlation coefficient revealed that the intra- and inter-observer variability of the proposed approach introduced by the user initialization was small, indicating good reproducibility, independent of different users. (E-mail: qiu.wu.ch@gmail.com)

Key Words: **Ventricular system segmentation, 3-D ultrasound imaging, Preterm neonate, Convex optimization, Intraventricular hemorrhage.**

INTRODUCTION

Neonates of very low birth weight (<1500 g) are surviving at increasing rates as prenatal and antenatal care has improved (Goldenberg et al. 2008). However, among this population, spontaneous brain bleeds in and around the lateral ventricles, known as intra-ventricular hemorrhage (IVH), occur often (in 12%–20%) (Martin et al. 2010) and have been linked to brain damage and morbidities such as cerebral palsy and developmental delay in later life (Wilson-Costello et al. 2005). More severe bleeds are correlated with more pronounced ventricular dilation (ventriculomegaly), which requires treatment when progressing to hydrocephalus and potential neurologic deficits later in life (Brouwer et al. 2008, 2012). Monitoring post hemorrhagic ventriculomegaly in a quantitative manner may assist clinicians in their decisions as to whether or not to intervene in patients

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presenting with large ventricles. Specifically, serial ventricle volume measurements could indicate whether or not a patient has a problematic increase in ventricle size.

Typically, the diagnosis of IVH is performed and graded using two-dimensional (2-D) clinical ultrasound (US) (Papile et al. 1978). The selection of brain slices imaged with 2-D US is dependent on operators because of the blurred location of the hemorrhage. Additionally, 2-D US is not capable of quantifying accurately the volume of irregular structures such as the ventricular system, including two lateral ventricles and the third and fourth ventricles (Damasio 2005). In contrast, 3-D US is found to be feasible in a clinical setting, can provide accurate quantitative ventricle volume size and can be used to monitor the neonatal ventricular system at the bedside (Abdul-Khaliq et al. 2000; Haiden et al. 2005; Kishimoto et al. 2013; McLean et al. 2012; Nagdyman et al. 1999). Moreover, the volume of cerebrospinal fluid (CSF) from accurate ventricle volume measurements could provide an indicator of how much CSF could be taken out during interventional therapies, such as ventricle taps and drains. There is no standard for the amount that can be removed during these procedures, and it varies widely from clinician to clinician (Vanneste 2000; Verrees and Selman 2004). Recently, a motorized 3-D US system developed for cranial US scanning of preterm neonates was used for image acquisition (Kishimoto et al. 2013). This system was constructed to give centers with limited funding (such as those in the developing world) a more cost-effective alternative to commercially available systems, which often would require the purchase of a new system, transducer and software. However, the ventricles must be segmented in the image to attain the clinically relevant ventricle volume. Figure 1 illustrates manual segmentation of a typical neonatal ventricular system model from a 3-D US image, which includes two lateral ventricles and the third ventricle, but not the fourth ventricle, because it is usually not visible in 3-D US images. Although manual segmentation is an option, it is arduous and time consuming (>>35 min for one 3-D image) and requires much expertise, making this approach clinically not feasible (Kishimoto et al. 2013). Therefore, an automated or semi-automated segmentation algorithm is highly desired to adequately reduce the time and workload required to obtain the ventricle volume from the 3-D US images in lieu of manual segmentation.

Cerebral ventricle segmentation algorithms have been developed for computed tomography (Liu et al. 2010; Poh et al. 2012; Qian et al. 2013) or magnetic resonance (Coupé et al. 2011; Jovicich et al. 2009; Liu et al. 2009; Schnack et al. 2001) images and used primarily in adult populations. Wang et al. (2011, 2014) proposed two automatic level set-based neonatal brain segmentation approaches, but their methods were applied to magnetic resonance images. Although studies have quantified 3-D US ventricle volumes in neonates (Haiden et al. 2005; Kishimoto et al. 2013; Nagdyman et al. 1999), all have used manually segmented regions. Unlike in a healthy neonate or an adult, segmentation of 3-D US images of a neonate with IVH poses unique challenges, because of the irregular shape deformation as well as poor image quality (Fig. 2), such as missing edges (Fig. 2b, e), inhomogeneities (Fig. 2a, d), US speckle, artifacts caused by patient movement, hyperechogenicity from blood clots and the highly vascularized choroid plexus (Fig. 2c, f). These challenges make most thresholding- or local optimization-based methods, such as active contour models (Kass et al. 1988) and level set methods (Chan and Vese 2001), not useful for this application. Difficulties are also encountered with automatic atlas-based segmentation approaches and include ventricular dilation and subsequent reduction of surrounding cerebral matter causing deformations to the structure, which cannot be easily accounted for and vary drastically from patient to patient, as illustrated in Figure 2. Another challenge in automatic atlas-based segmentation methods is that the third ventricle is not visible in some cases. This missing structure will lead to high

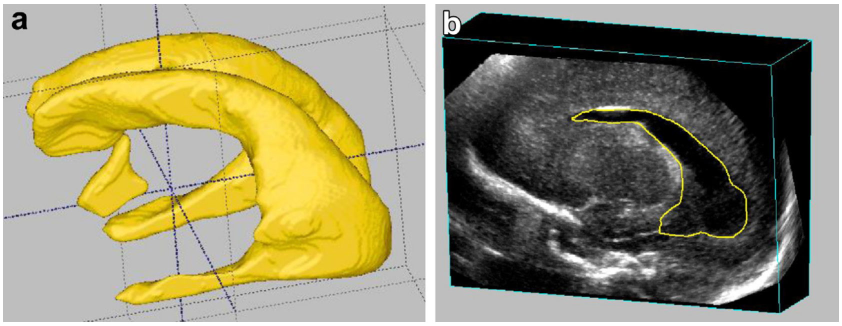

Fig. 1. Segmentation of a neonatal ventricular system model from a 3-D ultrasound image. (a) Segmented ventricular system model. (b) Original 3-D US image of ventricular system.