Neonatal Cerebral Ventricle Volume: A Comparison of 3D Ultrasound and Magnetic Resonance Imaging*

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Abstract

Enlargement of the cerebral lateral ventricles is observed in several neuropsychiatric disorders with origins in early brain development. Lateral ventricle size is also predictive of poor neurodevelopmental outcome in premature infants. 3D ultrasound offers an improved new methodology for the study of lateral ventricle volume in neonates. To assess the validity of ventricle volume measures obtained with 3D ultrasound, we compared the volumes obtained by 3D ultrasound with magnetic resonance imaging (MRI) in 7 neonates. Ventricle volumes were determined using a computer-assisted image analysis program, IRIS. There was excellent correlation between ventricle volumes obtained with 3D ultrasound and those obtained with MRI (Pearson $r = 0.96$, $p = 0.0005$) indicating that 3D ultrasound provides valid measures of overall lateral ventricle volume. 3D ultrasound can provide an economical and practical means studying lateral ventricle volume in neonates, a neurostructural marker of abnormal brain development.

Introduction

Mild enlargement of the lateral ventricles is found in neuropsychiatric disorders assumed to arise during pre- and perinatal brain development, including autism (Piven et al., 1995), idiopathic and syndromal mental retardation (Prassopoulos et al., 1996), fragile X syndrome (Reiss et al., 1995), Down's syndrome (Frangou et al., 1997), fetal alcohol syndrome (Swayze et al., 1997), and learning disorders (Sanderson et al., 1999) and schizophrenia (Lawrie and Abukmeil, 1998; Wright et al., 2000). We have hypothesized that the ventricle enlargement observed in these neuropsychiatric disorders can be detected very early in brain development with ultrasound (Gilmore et al., 1998, Gilmore et al., 2000a, Gilmore et al., 2000b). With a better understanding of normal and abnormal lateral ventricle size in the neonate, it may ultimately be possible to identify children at high risk for neurodevelopmental disorders.

Very little is known about lateral ventricle size and structure the neonate. Levene (1981) found that lateral ventricle width in a coronal scan measured through the temporoparietal bone increased with increasing gestational age at birth, but did not change significantly in the first 6 months of life. In contrast, Saliba et al. (1990) studied ventricle area in a coronal section of the occipital mid-body of the lateral ventricles over the first year of life in premature infants and found it to increase rapidly in the first 10 weeks after birth and more slowly thereafter. Shah et al., (1992) found that lateral ventricles width increased from 6.6 ± 3.2 mm at one month of age to 10.72 ± 2.92 mm at 6 months of age. Prior ultrasound studies of ventricle size are limited due to limited resolution of older ultrasound technology and inconsistent anatomic localization of two-dimensional (2D) width determinations. A recent MRI study of brain development in premature and normal newborns found no clear changes in total CSF volumes from 29 to 41 weeks; however ventricular and extracerebral CSF volumes were not separated (Huppi et al., 1998).

Most ultrasound studies of lateral ventricle size in the premature infant and normal newborn are limited to subjective descriptions of size or a 2D measure of width through one section of the lateral ventricle. Three-dimensional (3D) imaging of the lateral ventricle offers the potential to provide more accurate and detailed assessment of size and shape of this complex structure. 3D ultrasound has been used to image ventricles in human embryos as early as 7 weeks gestational age (Blaas et al., 1995, 1998). Systematic 3D ultrasound studies of neonatal ventricle volumes have not been performed, though recently Nagdyman et al. (1999) found that head position influences left/right ventricle volume differences in premature infants, but did not effect overall ventricle volume.

2D ultrasound has been shown to provide an accurate assessment of ventricle size compared to pneumoencephalography and computerized axial tomography (Lombroso et al., 1968, Johnson et al., 1979; Skolnick et al., 1979). Brann et al. (1990), developed a cylindrical coordinate system to estimate ventricle volume based on 2D ultrasound imaging, though this method has not been extensively validated and is not widely used. Studies with 3D ultrasound indicate that it provides accurate and reliable volume measures of phantoms (Riccabona et al., 1996; Hosli et al., 1998). To further assess the validity of 3D ultrasound measures of lateral ventricle volume in neonates, we compared volumes obtained by 3D ultrasound to those obtained by MRI in the same infant.

Methods and Materials

Ten neonates were recruited from our ongoing studies of prenatal isolated mild ventriculomegaly and the offspring of mothers with schizophrenia. After obtaining informed consent from a parent or guardian, the infants underwent a 3D cranial ultrasound and an MRI. The ultrasounds were done with a Medison Voluson 530D (Pleasonton, CA) using a 5/8 MHz neonatal sector transducer through the anterior fontenelle probe positioned in the midline

between the frontal horns of the lateral ventricles. An anterior to posterior sweep by the mechanical transducer in the probe captures the entire ventricle system in a few seconds. The MRI was done on a G.E. 1.5 T scanner at the Duke-UNC Neuroimaging Center using a 3D IR prepped fast SPGR with 1.5 mm thick slices. For the MRI, infants were scanned unsedated, swaddled, typically in the evening after being fed, with head fixed in a vac-fix device. In one infant, a head MRI obtained while the infant was sedated for a spinal MRI, done for clinical reasons.

Ultrasound data was reconstructed to a cartesian volume using software provided by the manufacturer (Softmax). The reconstructed ultrasound image data and MRI data was transferred to a UNIX workstation. Segmentation of the left and right lateral ventricles and determination of ventricle volumes was done with IRIS - an interactive image segmentation program developed at the University of North Carolina at Chapel Hill. The IRIS program allows region drawing arbitrarily on orthogonal cross sections and provides a three-dimensional graphical rendering of the volumetric object with the possibility to navigate between voxels in the volumetric image and the 3D graphics.

Results

We were unable to obtain a usable MRI scan on 3 children due to significant movement. The age at ultrasound for the seven children with usable US/MRI pairs was 45.6 ± 21.1 days (mean ± SD); mean interval between 3D ultrasound and MRI was 18.6 ± 22.9 days (mean ± SD). There was good correlation between individual ventricle volumes obtained with 3D ultrasound and those obtained with MRI (Pearson $r = 0.96$, $p = 0.0005$; see **Figure 1**). Intraclass correlation coefficient was 0.92 ($F = 23.28$, $p = 0.00027$). Each US/MRI pair had very similar volumes except in subject 7 in which the 3D ultrasound volume was approximately 75% of the

MRI volume. In this subject, time between scans (26 days), and acoustic blurring of midline aspects of the relatively large frontal horns in the ultrasound may account for this difference. **Figure 2** depicts volumes of left and right ventricles for each subject. **Figure 3** is an axial slice of the 3D ultrasound and MR images indicating that 3D ultrasound and MRI provide similar information about ventricle size and structure at this level.

Discussion

This study indicates that 3D ultrasound provides a valid measure of lateral ventricle volume in neonates, very similar to that obtained with MRI. This study also highlights the advantages of 3D ultrasound in the study of ventricle size in neonates. Compared to MRI, 3D ultrasound is far less expensive, requires much less set-up and scanning time, and is far less prone to motion artifacts that we found in 30% of the unsedated neonates that underwent MRI. These attributes make 3D ultrasound ideal for research studies that require multiple assessments of ventricle volume over time and for studies of the relationship of neonatal ventricle volume to neurodevelopmental outcome in large high risk cohorts.

3D ultrasound assessment of ventricle volume may also be useful in the prediction of risk for poor neurodevelopmental outcome in premature infants. Prior 2D ultrasound studies of lateral ventricle size in the premature infants indicate that ventricular enlargement is predictive of risk for poor neurodevelopmental outcome (Stewart et al., 1987; Costello et al., 1988; Roth et al., 1993; Leviton and Gilles, 1996). Children with low birth weight and subjectively defined persistent moderate enlargement of any ventricle on postnatal ultrasound (with or without associated parenchyma lesions) are at high risk for mental retardation and neuropsychiatric disorders at age 6 (Whitaker et al., 1996; Whitaker et al., 1997). Recently, it has been shown that ventriculomegaly in premature infants was an important predictor of IQ <70 at 4.5 years of age (Ment et al., 1999).

A significant portion of premature infants with clinically normal neonatal ultrasounds have neurologic and cognitive abnormalities that affect quality of life and probably risk for subsequent neuropsychiatric disorders. Fazzi et al. (1997) found that 50% of very low birth weight children with clinically "normal" cranial ultrasounds (normal or uncomplicated periventricular hemorrhage) had "minor sequelae" (minor neurologic deficits, low cognitive index scores) at age 5-7. Jongmans et al. (1997) found that 44% of premature children with clinically normal cranial ultrasounds had minor neurological or perceptual-motor problems at age 6. Finally, Stewart et al., (1999) found that 51% of premature infants with a normal (including uncomplicated periventricular hemorrhage) ultrasound had abnormal MRI's at 14 years of age, including ventricular enlargement. We hypothesize that better definitions of normal and abnormal ventricle size and shape obtained with 3D ultrasound will improve our ability to predict outcome in premature infants as well as in other high risk groups. Indeed a recent study of lateral ventricle volume in children with periventricular leukomalacia (PVL), found that larger ventricle volume was associated with more severe motor and cognitive deficits (Melham et al., 2000); the authors concluded that "lateral ventricle volume measurements can be used as quantitative markers of severity of clinical impairment and as predictors of clinical outcome in children with PVL before formal testing is possible."

In summary, 3D ultrasound provides a valid assessment of neonatal lateral ventricle volume. Further studies are necessary to determine the usefulness of 3D ultrasound in the study of neonatal lateral ventricle volume. We are currently performing a more detailed comparison of ultrasound and MR derived lateral ventricle segmentations, to determine whether differences the image aquistion modalities result in shape differences. 3D ultrasound can provide an economical

and practical means studying lateral ventricle volume, a neurostructural marker of abnormal brain development in high risk neonates.

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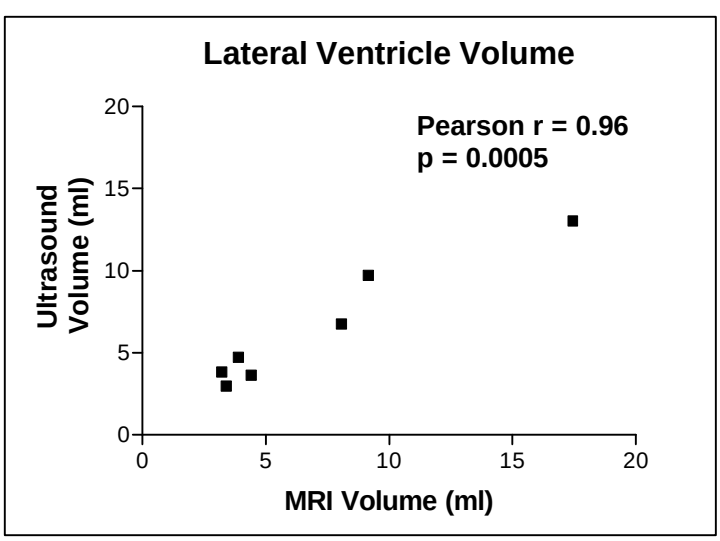


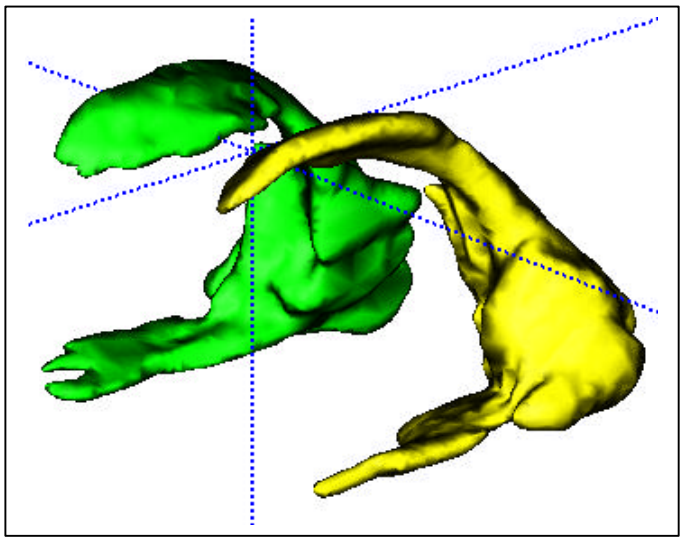
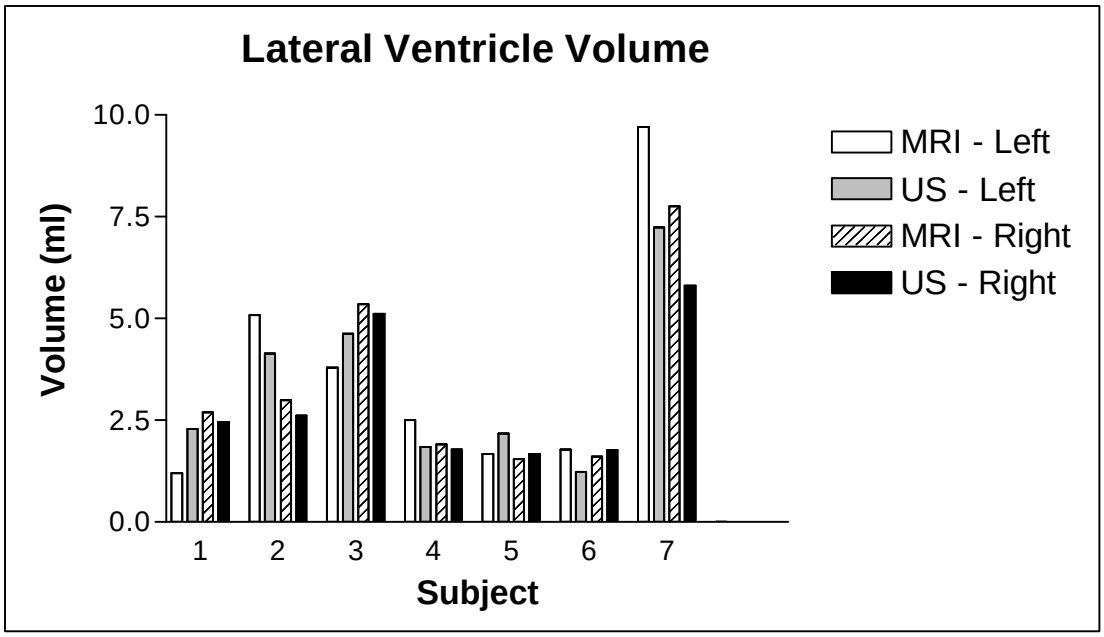


Figure 2



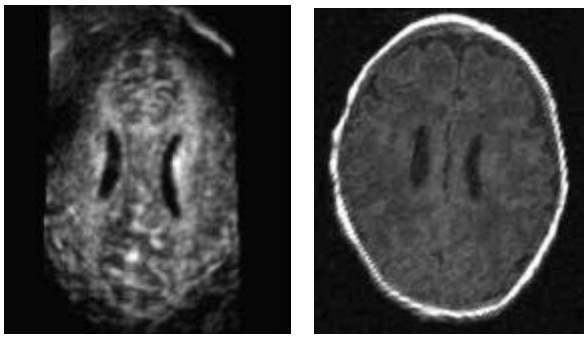


Figure 3: 3D Ultrasound (left) and MRI (right) in the same neonate.