Original Article

Diagnostic Effectiveness of Three-Dimensional Ultrasonographic Imaging of Pediatric Brain

Kriengkrai Iemsawatdikul MD[1], Preeyacha Pacharn MD[1], Nucharree Chotipanvittayakul BSc, RT[1], Chirawat Sudla BSc, RT[1]

[1] Division of Diagnostic Radiology, Department of Radiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Background: Three-dimensional cranial ultrasonography [3DCUS] is a new developing technology that provides fast scanning time and image post processing ability. However, its image quality and diagnostic value are still questionable for clinical usage.

Objective: To evaluate the diagnostic effectiveness and image quality of 3DCUS compared to the two-dimensional cranial ultrasonography [2DCUS].

Materials and Methods: The present study was done prospectively in 175 cranial ultrasound examinations. Each examination consists of 2DCUS and 3DCUS images taken at the same session. Each set of data was reviewed by two pediatric radiologists for diagnosing of intracranial abnormalities and evaluating image quality in several intracranial regions. By using 2DCUS as a gold standard, the effectiveness and image quality of 3DCUS were assessed. The study protocol was approved by the Ethics Committee of Faculty of Medicine Siriraj Hospital, Mahidol University (Si577/2009).

Results: The 2DCUS demonstrated significant higher image quality in most of intracranial regions except occipital lobe (p = 0.07), midbrain (p = 0.13) and pons (p = 0.16). The 2DCUS also showed better demonstration of the intracranial lesions such as intraventricular hemorrhage, hydrocephalus, cerebral white matter lesions, cerebellar abnormalities and extracranial lesions. However, there was no significant difference in diagnostic capability between these two modalities.

Conclusion: Although Image quality of 3DCUS examination is inferior to that of 2DCUS, it is sufficient to diagnose intracranial abnormalities in clinical practice.

Keywords: Two-dimensional ultrasound, Three-dimensional ultrasound, Cranial ultrasound, 2D, 3D

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Cranial ultrasonography [CUS] plays an important role in neonatal and infant care. It is frequently used for evaluation of intracranial hemorrhage. It can demonstrate not only anatomic abnormality but also hemodynamic information through Doppler study. Its common indications include screening intraventricular hemorrhage [IVH], evaluating hydrocephalus, and evaluating intracranial anomaly.

Other benefits of CUS are portability and lack of radiation. CUS can be performed as a bedside study, suitable for critically ill neonates and infants who cannot be moved to computed tomography or magnetic resonance imaging units. Because CUS is a radiation-free examination, it is a study of choice for close follow-up intracranial conditions.

Two-dimensional cranial ultrasonography [2DCUS] was first introduced in 1970. During the past 40 years, its diagnostic accuracy has been improving dramatically by the advent of new technologies including high-frequency, miniature transducers, fast computer processors, and contrast agent usage[1]. However, it still has several unsolved limitations. First, 2DCUS are series of non-contiguous, presumably representative section of the imaged organ to demonstrate its entire complex anatomy. It is an operator-dependent modality. In a case of inexperienced sonographers who fail to pick up pathology during the scan, these lesions are impossible to be detected on documented images, and then repeat examinations are required. Second, the imaging planes are fixed during examination and are impossible to be reconstructed to other planes. To obtain specific plane such as the axial plane on CUS, one has to readjust the infant's head position for temporal or mastoid approaches, which could increase the risk of tube, line malposition, and instrument malfunction. Third, comparison of the serial examinations is difficult because exactly

Correspondence to:

Iemsawatdikul K. Division of Diagnostic Radiology, Department of Radiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.
Phone: +66-2-4197000
Email: k4400559@gmail.com

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corresponding planes are rarely acquired. Forth, volume rendering and surface rendering are impossible to be reconstructed from two-dimensional dataset. Finally, its long scanning time increases the risk of infection and hypothermia[2].

Three-dimensional cranial ultrasonography [3DCUS] was first used in clinical practices and researches in the fetus[3]. Now, its applications in gynecology, neurology, neurosurgery, urology, and interventional radiology are being evaluated[4-10]. By using special mechanical driven volume transducer, the scan is performed by automatically sweeping over a pre-defined area. The 3D raw data are completely acquired in less than ten seconds. These kinds of dataset can be reconstructed into specific imaging planes (coronal, sagittal, axial, and oblique), or can be manipulated by post-processing software (gain control, adjust slice thickness, zoom, pan, surface/volume rendering, volume measurement) to enhance diagnostic accuracy[11].

There are few investigators who have studied the clinical application of 3DCUS[11,12]. Most of the studies mentioned about the potential clinical applications of this modality without statistical supporting evidence. Only one study published by Salerno et al showed the systematic comparison between the diagnostic value of 2DCUS (hard copies) and that of 3DCUS (hard copies and digital images)[12]. With improving 3DCUS technology and increasing usage of picture archiving and communication system [PACS], the author assumes that image quality and diagnostic accuracy from current system could be improved substantially from those in the previous publications.

The purposes of the present study were to evaluate the effectiveness of 3DCUS and compare its image quality to that of 2DCUS.

Materials and Methods

The present study protocol was approved by the Ethics Committee of Faculty of Medicine Siriraj Hospital, Mahidol University (Si.577/2009). All scanning processes, risks benefit, and data privacy were explained to the patient's parents or guardians. The informed consents were obtained from patient's guardians.

The primary outcome of the present study was to evaluate the image quality of 3DCUS compared to that of 2DCUS. Based on previous studies and investigators' experience, it was estimated that 2DCUS and 3DCUS would yield excellent/adequate quality of 95% and 85%, respectively[12]. Using a sample size formula for McNemar's test, a 2-sided type I error of 0.05, 80% power, a sample of 173 was required to detect 10% difference and 23% discordance.

The present study was performed prospectively between February and October 2010. The assigned radiologists performed both 3DCUS and 2DCUS with Logiq 9 (GE Healthcare, Little Chalfont, UK) in neonates and infants who were scheduled for 2DCUS in the outpatient section of the radiology department. The indications for the imaging included screening for IVH, to follow previously diagnosed IVH, to rule out hydrocephalus, to follow-up previously diagnosed hydrocephalus, and to rule out intracranial anomalies. All patient's demographic data (age, gestational age, size of anterior fontanel, and closure of temporal/mastoid sutures) were recorded. All the examinations started with 2DCUS, which was performed first, followed immediately by 3DCUS.

The 2DCUS examinations was performed with the microconvex transducer (8.5 megahertz) and the convex transducer (5.0 megahertz). The 2DCUS examination consisted of six coronal, five sagittal images via anterior fontanel approach, two sagittal images via posterior fontanel approach, and four axial images via temporal and mastoid approaches. The 3DCUS examinations, performed with 3D convex transducer (5.0 to 7.5 megahertz), consisted of volumetric data scanned from anterior fontanel approach. The scanning process included automatic motorized mechanically sweep in coronal orientation (from anterior to posterior aspect) and sagittal orientation (from right to left side).

All the examinations' images were divided into two datasets. The first dataset consisted of 2D images, and the other consist of 3D volumetric data. The 2D images were sent to hospital's routine PACS (Synapse, FUJIFILM Corporation, Tokyo, Japan), while 3D volumetric data were sent to the independent server built specifically for the present research.

The images from 2DCUS and 3DCUS examinations were reviewed separately by the two pediatric radiologists with 16 to 17 years experience (Iemsawatdikul K and Pacharn P). All the images were assigned to radiologists for reading in random order. While radiologists reviewed images from each data set, they were not allowed to see the images from the other data set. The radiologists were assigned to record information including date of interpretation, scanning time, gestational age, patient's age, size of anterior fontanel. To assess image quality, the radiologists were assigned to record image quality in the specific area (frontal, parietal, temporal, occipital lobes, corpus

callosum, thalamus, midbrain, pons, cerebellar vermis, and cerebellar hemisphere). The image quality was classified into excellent (the image quality is good with clearly demonstrate intracranial structure or lesion), adequate (the image quality is good enough to identify intracranial structure or lesion) and inadequate (the image quality is not good enough to identify intracranial structure or lesion). To assess diagnostic accuracy, the radiologists were assigned to record one or two final diagnoses such as the presence or absence of IVH, hydrocephalus, abnormal cerebral echogenicity, and abnormal cerebellar echogenicity. The radiologists were encouraged to give the most specific diagnosis if possible such as holoprosencephaly or agenesis of corpus callosum, etc. For diagnosing hydrocephalus, ventricular index is used by comparing to normal value for age[13]. In the case of positive IVH, the severity grade of the lesions must be recorded by using Papile and Burstein classification[14]. While radiologists reviewed 3D image dataset with image processing software (Viewpoint, GE Healthcare, Little Chalfont, UK), they were allowed to use special post-processing image manipulation including gain control, thickness adjustment, tomographic ultrasound imaging [TUI], surface/volume rendering, coronal/sagittal/axial, and oblique plane reconstruction.

The datasets were reviewed in two sessions, separated by a minimum of three months, with the 2DCUS images data set reviewed first, to eliminate any memory bias. If there were discrepancies among readers, the images were re-evaluated by all radiologists to make the final agreement.

Statistical analysis

Weighted kappa statistics was (quadratic weight) was used to evaluate the inter-observer agreement.

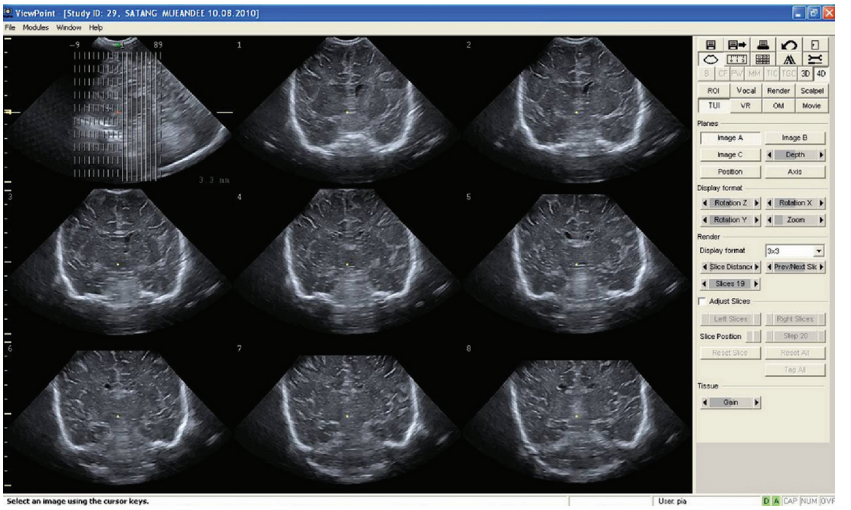
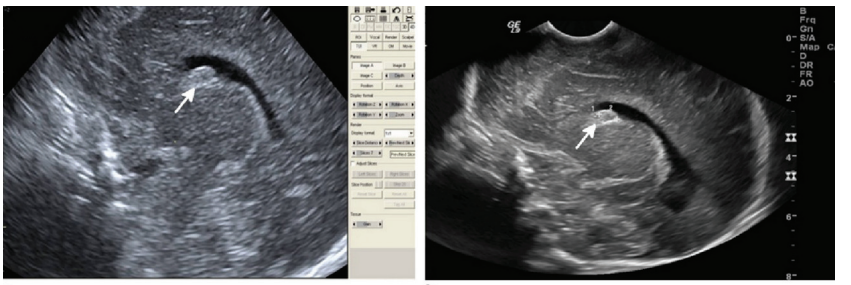


Figure 1. A screen capture image from workstation (Viewpoint software) demonstrates tomographic ultrasound images from a 5-day-old premature neonate. On the right panel, there are several tools for image processing such as gain/slice thickness control, surface/volume rendering and volume measurement.



a **b**

Figure 2. A sagittal reformatted image from the 3D dataset of 3DCUS (a) and a sagittal image from 2DCUS (b) of a 3-day-old premature neonate born at 28-week gestation. Although 3DCUS image shows lower resolution than that of 2DCUS, grade I intraventricular hemorrhage (arrows in a and b) can be confidently diagnosed on both images.

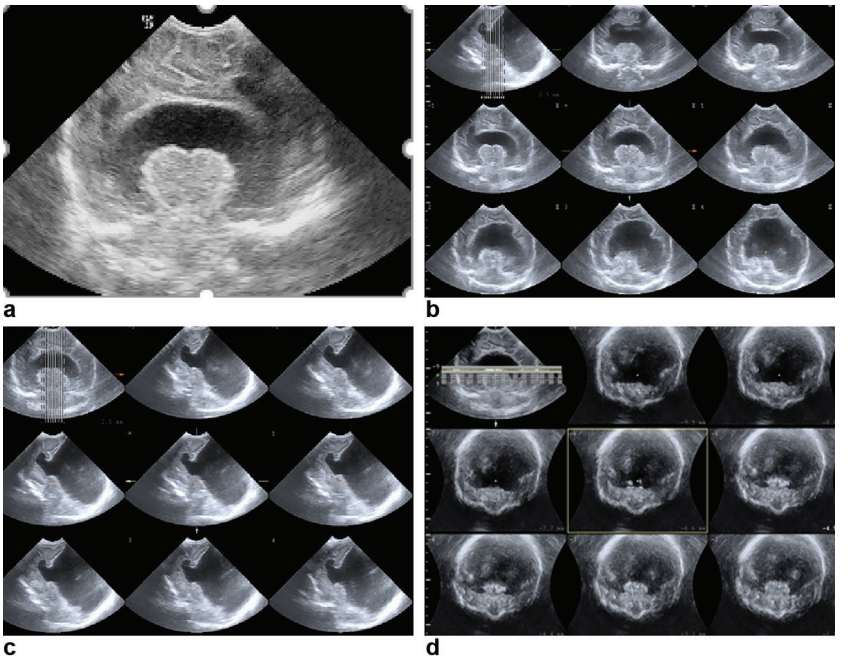


Figure 3. A 10-day-old premature neonate presented with dysmorphic features. The cranial ultrasound shows classic alobar holoprosencephaly. (a) A coronal image from 2DCUS, (b-d) Coronal TUI images with sagittal and axial reformat from the 3D dataset (c and d, respectively).

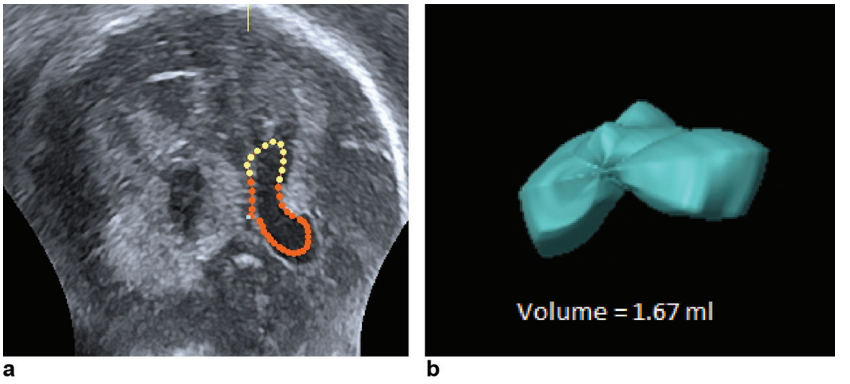


Figure 4. A 3-day-old premature neonate with mild hydrocephalus. (a) An axial reformat image reconstructed from the 3D dataset. The dotted line was manually drawn on the workstation to outline border of the lateral ventricle. (b) The 3D volume rendering image and volume calculation of the lateral ventricle created by software according to the dotted line drawn (a).

McNemar's test was used to evaluate the differences of IVH grades, hydrocephalus (in term of presence or absence) between 2DCUS and 3DCUS. Wilcoxon test was used to evaluate the difference between the quality of image (in individual areas) and the diagnostic capability (in term of presence or absence of disease) between 2DCUS and 3DCUS. All analyses were performed with IBM SPSS Statistics for Windows version 20.0 (IBM Corp. Armonk, NY, USA). A *p*-value smaller than 0.05 was considered a statistically significant difference.

Results

The present study consisted of 175 patients. Ninety-seven were boys, and 78 were girls. Mean gestational age was 232.9±26.1 days (168 to 288 days). Mean postnatal age was 48.9±61.1days (4 to 500 days). Mean post-conceptual age was 281±66.1 days (201 to 710 days). Mode of gestational age, postnatal age, and post-conceptual age were 231,

15, 246 days, respectively. Median gestational age, postnatal age, and post-conceptual age were 231, 33, 260 days, respectively. Mode and median for fontanel's size were two fingerbreadths (size range from 1 to 4 fingerbreadths).

The most common indication was to screen for IVH (n = 88), followed by follow-up of known IVH (n = 32). Other indications included to evaluate intracranial anomaly (n = 24), hydrocephalus (n = 22), brain parenchymal hemorrhage (n = 5), intracranial infection (n = 2) and to follow-up known periventricular leukomalacia (n = 2).

There were 52 cases of IVH (grade I 47 cases, grade II 1 case, grade III 2 cases, grade IV 2 cases). Other intracranial abnormalities included choroid plexus cyst (n = 9), asymmetry of the lateral ventricle (n = 6), brain atrophy (n = 5), external hydrocephalus (n = 4), lenticulostriate vasculopathy (n = 3), periventricular leukomalacia (n = 3), agenesis of corpus callosum with interhemispheric cyst (n = 2), pineal cyst (n = 2), schizencephaly (n = 2), alobar holoprosencephaly (n = 1), brachycephaly (n = 1), Chiari II malformation (n = 1), choroid plexus papilloma (n = 1), ectasia of superior sagittal sinus (n = 1), encephalomalacia (n = 1), lobulated choroid plexus (n = 1), old lacunar infarction (n = 1), and pineal tumor (n = 1). Information regarding IVH is listed in Table 1, and other abnormal findings are listed in Table 2.

The mean scanning time of 3DCUS (41.8 seconds) was significantly shorter than that of 2DCUS (164.3 seconds, *p*-value <0.001).

There was excellent agreement among two readers (weighted kappa coefficients for grading of IVH on 2DCUS and 3DCUS were 0.92 and 0.90, respectively).

There was no significant difference between the grades of IVH diagnosed by 2DCUS and 3DCUS (*p*-value 0.48). There were four examinations that showed discrepancies between both modalities. On two of these examinations, 2DCUS were diagnosed as negative while 3DCUS were diagnosed as IVH grade I. On the other two, 2DCUS were diagnosed as IVH grade I while 3DCUS were diagnosed as negative.

There was no significant difference between hydrocephalus diagnosed by 2DCUS and 3DCUS in term of presence or absence (*p*-value 0.375). There were eight examinations that showed discrepancies between both modalities in diagnosing hydrocephalus. By using 2DCUS as a gold standard, 3DCUS showed sensitivity, specificity, positive predictive value, negative predictive value at 97.5%, 58.3%, 96.9%, 63.6%, respectively with false positive in four examinations and false negative in the other four.

Table 1. Intraventricular hemorrhage stratified by grade (n = 52)

Grade of IVH	Number of patients (% of total patients)
I	47 (26.9)
II	1 (0.6)
III	2 (1.1)
IV	2 (1.1)
Total	52 (29.7)

IVH = intraventricular hemorrhage

Table 2. List of intracranial abnormal findings (n = 46) other than IVH

Abnormal findings	Number of patients (% of total patients)
Choroid plexus cyst	9 (5.1)
Asymmetry of lateral ventricle	6 (3.4)
Brain atrophy	5 (2.9)
External hydrocephalus	4 (2.3)
Lenticulostriate vasculopathy	3 (1.7)
Periventricular leucomalacia	3 (1.7)
Agenesis of corpus callosum with interhemispheric cyst	2 (1.1)
Pineal cyst	2 (1.1)
Schizencephaly	2 (1.1)
Alobar holoprosencephaly	1 (0.6)
Ectasia of superior sagittal sinus	1 (0.6)
Brachycephaly	1 (0.6)
Chiari II malformation	1 (0.6)
Choroid plexus papilloma	1 (0.6)
Encephalomalacia	1 (0.6)
Loculated choroid plexus	1 (0.6)
Old lacunar infarction	1 (0.6)
Pineal tumor	1 (0.6)
Frontal horn cyst	1 (0.6)
Total	46 (26.3)

IVH = intraventricular hemorrhage

There was 100% match between these two modalities in diagnostic findings other than IVH and hydrocephalus.

There were significant differences in images quality between the two modalities in most intracranial regions, except in occipital lobe, midbrain, and pons. Subgroup analysis was performed in the patient with large size fontanel (larger than three finger breadths). There were no significant differences in images quality in all intracranial regions. Information regarding imaging quality comparison is listed in Table 3.

Discussion

The 3DCUS is a new technology that facilitates

Table 3. Quality comparison between 2DCUS and 3DCUS (n = 175)

Location	All patients (n = 175) *p*-value	Patient with size of anterior fontanel ≥3 finger breadths (n = 35), *p*-value
Frontal lobes	0.001	0.046
Parietal lobes	0.005	0.48
Temporal lobes	0.018	0.157
Occipital lobes	0.07	0.129
Corpus callosum	0.019	0.257
Thalamus	0.02	0.206
Midbrain	0.13	0.132
Pons	0.167	0.52
Cerebellar vermis	0.001	0.822
Cerebellar hemisphere	0.001	0.66

CUS = cranial ultrasonography

scanning and image interpreting processes. By collecting data as volume, one can perform the scan rapidly without missing any information. Some lesions can be better demonstrated and easily be understood by using post-processing image manipulation (TUI, volume/surface rendering, multiplanar reconstruction, gain, and slice thickness adjustment). Temporal and mastoid approaches can be replaced by using image reconstruction to the specific plane (such as axial reconstruction). In addition, an accurate comparison between one to other studies is possible because the exact imaging planes can be created by post-processing technique.

The previous study performed by Salerno et al[12] (n = 59) showed that the mean scanning time of 3DCUS (1.7±0.7 minutes) was significantly shorter than that of 2DCUS (9±4.5 minutes). The study of Junewick et al[15] (n = 17) showed mean scanning time of 2DCUS was 10.26 minutes and that of 3DCUS was 1.51 minutes. The present study agreed with these previous studies.

Salerno et al[12] have compared the diagnostic value of 2DCUS images (hard copy images) and 3DCUS images (hard and soft copy images) in evaluating IVH, developmental abnormality, abnormal increased echogenicity, intracranial cyst, and extra-axial fluid. They reported no difference between these three types of imaging in detecting and grading these lesions. The present study confirmed the result of this study.

In the present study, there were four examinations that showed minor discrepancies between 2DCUS and 3DCUS images in grading IVH (3DCUS misdiagnosed grade I IVH as negative in two cases and over diagnosed negative case as grade I IVH in the other two). In clinical practice, these two categories are difficult to be accurately defined and have very high inter/intra-observer variation[16-18]. Fortunately, misclassification between grade I and grade II IVH has no clinical significance[19,20].

There were eight examinations that showed discrepancies in diagnosis hydrocephalus between 2DCUS and 3DCUS. In the author opinion, 2DCUS is less accurate than 3DCUS in diagnosing this condition and unsuitable to be a gold standard. Gilmore et al[21] compared lateral ventricle volumes measured by 3DCUS with those measured by magnetic resonance imaging of the brain. They found an excellent correlation between these two modalities. Their study supported the result of the present study that the discrepancies between these two modalities most likely from the inaccuracy of 2DCUS itself rather than the diagnostic error of 3DCUS.

There was 100% match between these two modalities in diagnostic findings other than IVH and hydrocephalus. Due to the diversity of intracranial abnormalities in the present study comparing to the previous study[12], the present study not only confirmed their result but also confidently concluded that 3DCUS can replace 2DCUS in clinical practice.

The images from 2DCUS showed significant superior quality than those of 3DCUS in most intracranial anatomic zones except areas of the occipital lobe, midbrain, and pons. The reason is that the 2D transducer used in the present study has the higher frequency than that of the 3D transducer, making it possible for 2DCUS to capture better resolution images. Another explanation is the small footprint of the 2D transducer providing a better chance to fit into small fontanel. Conversely, the bulky appearance of the 3D transducer is susceptible to an artifact from bony parts of the skull. There was no significant difference in image quality between 2DCUS and 3DCUS in areas of the occipital lobe, midbrain, and pons. In the author opinion, pons and midbrain locate in the center of the cranium. It takes long distance for sound beams to travel from all acoustic windows to the target areas. The image qualities from both 2DCUS and 3DCUS are relatively low in comparison to other anatomic regions. This was the reason why there was no quality difference between images from both modalities. Although the posterior fontanel approach is an alternative method to image occipital lobe, it is relatively too small for most transducers to capture a good quality image. Although 2D transducer has higher resolution and needs a smaller footprint, it cannot not capture better images to make a significant difference from those obtained from the 3D transducer.

Size of fontanel has a significant impact on image quality. When scanning through relatively small fontanel or scanning with large transducer, image quality can be degraded by artifact from bony edges of the skull. Subgroup analysis performed in the patient who had large anterior fontanel (≥3 finger-breadths, n = 35) showed no significant differences in images quality between 2DCUS and 3DCUS in all intracranial anatomic zones. The author suggests that 3DCUS, when used in patients with large anterior fontanel, can provide image quality equal to that of 2DCUS.

Cinegraphic images refer to images obtained by manual sweeping the transducer and digitally saved as movie file for later analyzation. It has relatively short scan time (1.2 to 6.5 minutes) when compared to static imaging. O'dell et al[22] have compared cinegraphic images with combined static/cinegraphic images in 140 premature neonates. They reported that CUS screening by using cinegraphic imaging alone is a potentially advantageous option in the initial intracranial evaluation in premature neonate. Because the images obtained by cinegraphic scan and 3DCUS are quite similar when displayed on work station, the present study supports the result of that study.

There were several limitations in the present study. First, the study population was limited to neonates and infants who could be transferred to ultrasound units. The author did not include patients who were admitted to neonatal intensive care unit because the ultrasound machine was difficult to be moved from one hospital building to another. Because the patients in neonatal intensive care unit are relatively young and have large anterior fontanels, large size 3D transducer does not affect image quality. The author assumed that the quality of the image from 3DCUS should be equal to those from 2DCUS while scanning these patient population. Second, the present study evaluated most intracranial abnormalities in term of presence and absence, except for IVH evaluation. The specific details of abnormalities (such as details of specific intracranial anomalies, types of schizencephaly, or sizes of choroid plexus papilloma) are beyond the scope of the present study. Third, the present study was performed with single specific ultrasound model (Logiq 9, GE Healthcare, Little Chalfont, UK). The outcome from this machine model could not directly predict results from other models.

Three-dimensional ultrasound has a bright future in clinical practice. In the present study, 3DCUS was adequate in diagnosing intracranial abnormality with acceptable image quality. With the ease of use and steep learning curve, the 3D dataset can be performed by ultrasound technicians, attending nurses, or primary physicians, then transferred digitally to radiologists' workplace. The health care workers will get benefit by increasing productivity, especially in busy hospitals. Alternatively, the dataset can be obtained and remotely transferred from rural areas to the medical center where radiologists are available for consultation.

Conclusion

Although 3DCUS provides inferior image quality than that of 2DCUS, it is sufficient to diagnose diversity of intracranial abnormalities in clinical practice.

What is already known on this topic?

3DCUS is a new developing technology that provides fast scanning time and image post processing ability. However, its image quality and diagnostic value are still questionable for clinical usage

What this study adds?

This study shows strong evidence that 3DCUS can replace 2DCUS in diagnosing intracranial abnormality.

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Potential conflicts of interest

The authors declare no conflict of interest.

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