

Structural linear measurements in the newborn brain: accuracy of cranial ultrasound compared to MRI

Lara M. Leijser · Latha Srinivasan ·
Mary A. Rutherford · Serena J. Counsell ·
Joanna M. Allsop · Frances M. Cowan

Received: 10 November 2006 / Revised: 2 March 2007 / Accepted: 3 March 2007 / Published online: 8 May 2007
© Springer-Verlag 2007

Abstract

Background Structural size in the neonatal brain is of clinical importance. Cranial ultrasonography (cUS) is the primary method used for evaluating the neonatal brain and it is important to know whether linear measurements made using this technique are accurate.

Objective To compare linear measurements of different cerebral structures made from neonatal cUS and contemporaneous MRI.

Materials and methods Preterm and term infants studies with cUS and MRI on the same day were studied. Linear measurements made using both techniques from many cerebral structures were compared using a paired *t*-test.

Results A total of 44 sets of scans from 26 preterm and 8 term infants were assessed. Small but significant differences between the cUS and MRI measurements ($P < 0.05$) were found for the ventricular index, the posterior horn depth of the lateral ventricle, the extracerebral space and interhemispheric fissure, and the cortex of the cingulate gyrus. No significant differences were found for any other measurements.

Conclusion Linear measurements from cUS are accurate for most neonatal cerebral structures. Significant differ-

ences compared to MRI were found for a few structures, but only for the cortex were the absolute differences marked and possibly of clinical importance.

Keywords Brain · Ultrasound · MRI · Newborn · Measurements

Introduction

Measurement of cerebral structures in the newborn infant brain can be of clinical importance for diagnosing cerebral abnormalities. Structural brain abnormalities can be quantified by performing linear measurements. Neuroimaging studies have shown that preterm infants at term-equivalent age have more subtle reduction in the size and maturation of many cerebral structures and an increased size of the lateral ventricles and cerebrospinal fluid volumes compared to term-born infants [1–4]. These differences between the preterm and term-born infant brain persist and are associated with less favourable neurodevelopmental outcomes for the preterm infant [1–5]. Several cranial ultrasound (cUS) and MRI studies on linear and volume measurements of different anatomical structures and tissues in the newborn infant and fetal brain are available in the literature [6–27]. These studies describe different techniques for performing the measurements on both cUS and MRI and give reference values for various cerebral structures [6–27].

It is generally considered that the measurements performed on cUS are consistent with those obtained from MRI, but few systematic studies have compared cUS with MRI and/or histological measurements of cerebral structures in the newborn infant or fetal brain [24, 26, 28]. Linear measurements of the height of the cerebellar vermis

L. M. Leijser · L. Srinivasan · F. M. Cowan (✉)
Department of Paediatrics, Hammersmith Hospital,
Imperial College, Du Cane Road,
London W12 OHS, UK
e-mail: f.cowan@imperial.ac.uk

L. Srinivasan · M. A. Rutherford · S. J. Counsell · J. M. Allsop ·
F. M. Cowan
Department of Imaging Sciences, Hammersmith Hospital,
Imperial College, Du Cane Road,
London W12 OHS, UK

performed on cUS were not found to be consistent with those performed on MRI [24]. As sequential cUS is still the most commonly used and preferable technique for the evaluation of the newborn infant brain in the neonatal period and linear measurements can easily be done at the bedside, it is important to know whether the linear measurements of cerebral structures performed on cUS are accurate.

The aim of this study was, therefore, to explore whether the linear measurements of different cerebral structures performed on neonatal cUS are accurate, by comparing them with those obtained from contemporaneous MRI in the preterm and term-born infant brain.

Materials and methods

Patients

During the study period (February 2005 to February 2006) preterm and term-born infants who underwent a cUS and MRI examination on the same day were included. All infants were examined prior to scanning [29, 30] and infant growth characteristics were recorded. The cUS was performed just before or after the MRI examination as part of the routine assessment of the infant. Ethical approval for studying the newborn infant brain using MRI was given by the Hammersmith Hospitals Research Ethics Committee and parental consent was obtained in each case. The MRI examinations were performed as part of ongoing research cohort studies of apparently well preterm and normal term-born infants. Other infants were scanned for different clinical indications, including moderate ventriculomegaly, hypoxic-ischaemic encephalopathy and suspected metabolic and neuromuscular disorders.

Exclusion criteria were major congenital anomalies or serious acquired abnormalities of the central nervous system, chromosomal disorders, metabolic disorders, neonatal meningitis, severe hypoxic-ischaemic damage and neonatal stroke. Thus we did not include infants with major cerebral abnormalities.

Neuroimaging

Ultrasonography

All cUS scans were performed by the same observer (L.M.L.), using a Siemens Antares US scanner with a multifrequency transducer (Siemens Medical Solutions, Bracknell, UK). Scanning was done in at least six coronal and five sagittal planes, using the anterior fontanelle as the acoustic window. The transducer frequency was set at 7.3 MHz. For detection of cortical and/or subcortical abnormalities, higher frequencies were used. For deeper structures or in relatively large infants, a

lower frequency was used. cUS scans were evaluated during and immediately after the procedure by the examiner and all scans were digitally stored and later evaluated by L.M.L. and F.C. Measurements were made later from the digitally stored images.

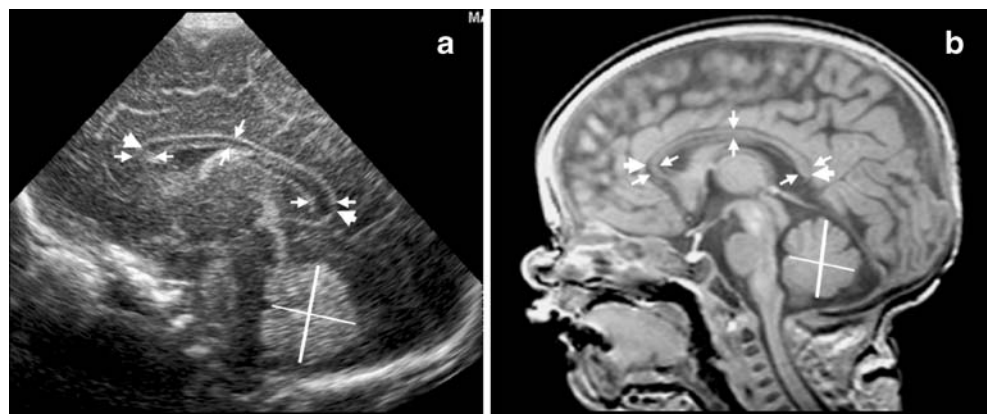
MRI

MRI was performed according to a standard MRI protocol for newborn infants using a 3.0-T Philips MR system (Philips, Best, The Netherlands). If needed, infants were given a sedative (oral chloral hydrate, 20–30 mg/kg), a safe and effective regimen [31]. They were laid supine and snugly swaddled. Ear protection comprised both individually moulded earplugs of a silicone-based putty (President putty, Coltene/Whaledent, Mahwah, N.J.) placed in the external ear and commercially available neonatal ear muffs (Natus MiniMuffs, Natus Medical, San Carlos, Calif.) placed over the ear. The head was stabilized using a pillow filled with polystyrene beads, from which the air was evacuated. The infant's temperature, heart rate and oxygen saturation were monitored throughout the procedure, during which a neonatologist experienced in resuscitation and MR procedures was always present. For this study, images obtained in the sagittal plane acquired using T₁-weighted MPRAGE sequences were used, but for all infants T₂-weighted (T₂-W), diffusion-weighted and often other sequences were also obtained. All MRI examinations were evaluated by two experienced observers (L.S. and M.R.) by consensus.

Linear measurements

All linear measurements on cUS were performed by L.M.L. using the software program Escape Medical Viewer (Escape Medical Imaging, Thessaloniki, Greece). The MR images were assessed using the software program ViewForum (Philips, Best, The Netherlands). With this program, different planes, including coronal and sagittal planes as obtained with cUS scanning, can be reconstructed, which enabled comparison of the cUS and MRI examinations. All linear measurements on MRI were performed by L.S. T₁-weighted MPRAGE images were used as they are 3D volume scans and can be reconstructed in any plane and have been shown to be more sensitive for accurate structural measures. For the linear measurements, digital callipers capable of measuring to within 0.1 mm for cUS and 0.2 mm for MRI were used. For comparing the measurements, the MR image most closely akin to the cUS plane in which the cUS measurement was performed was used. We accept that neither MRI nor cUS can be considered as absolute measurements for in vivo tissue structures, but MRI is probably the optimal imaging

Fig. 1 Measurements of the width of the genu, body and splenium (*thin arrows*) and length (*thick arrows*) of the corpus callosum and height (*thick line*) and AP width (*thin line*) of the cerebellar vermis in the mid-sagittal plane on cUS (a) and MRI (b)



modality we have for this purpose. Histological measurements are not available and post-mortem tissue is likely to be altered by change secondary to the cause of death and post-mortem artefacts.

cUS and MRI measurements were made on the following structures:

- The *corpus callosum*: the width of the genu, body and splenium and length in the mid-sagittal plane (Fig. 1).
- The *cerebellum*: the height and AP width of the vermis in the mid-sagittal plane and the maximum cerebellar hemispheric width in a coronal plane (Figs. 1 and 2).
- The *pons*: the AP width in the mid-sagittal plane (Fig. 3).
- The *lateral ventricles*: the ventricular index (VI) in the mid-coronal plane and the depth (thalamo-occipital distance) of the posterior horns in a parasagittal plane (Figs. 4 and 5).
- The *cavum septum pellucidum*: height and width in the mid-coronal plane (Fig. 6).
- The *fourth ventricle*: width in the mid-sagittal plane (Fig. 3).
- The *interhemispheric fissure* (IHF): width (maximum horizontal distance between the hemispheres, measured from the depth of sulci) in the mid-coronal plane (Fig. 6).
- The *extracerebral space* (ECS): height (shortest vertical distance between the calvarium and the surface of the cerebral cortex) in the mid-coronal plane (Fig. 6).
- The *cortex*: depth along the cingulate gyrus in a parasagittal plane, where the cortex is well defined running above and parallel to the mid of the corpus callosum (Fig. 7).
- The *basal ganglia*: maximum transverse width in the mid-coronal plane (Fig. 8).
- The *caudate heads*: maximum diagonal width in the mid-coronal plane (Fig. 8).

Most linear measurements on cUS and MRI were performed as described previously for newborn infants and fetuses [6–14, 19, 20, 22, 24]. For several linear measurements, no description was available in the literature. The width of the basal ganglia was measured from the midline of the brain to the most lateral border of the basal ganglia (i.e. lentiform nucleus), considered to be the most

Fig. 2 Measurement of the maximum cerebellar hemispheric width in a coronal plane (*line*) on cUS (a) and MRI (b)

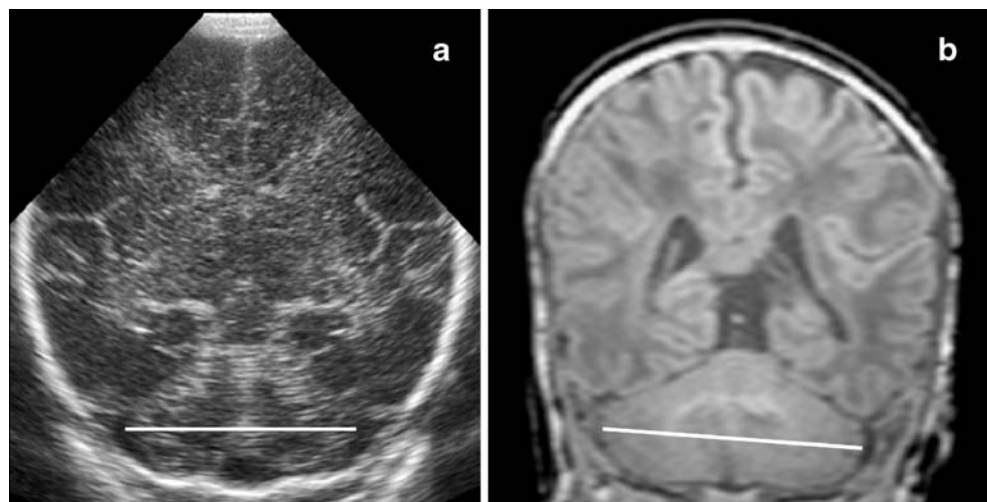
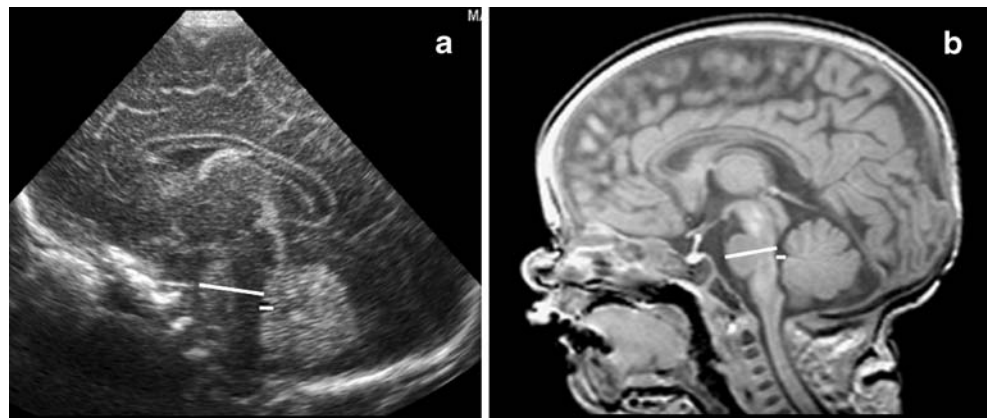


Fig. 3 Measurements of the AP width of the pons (*long line*) and the width of the fourth ventricle (*short line*) in the mid-sagittal plane on cUS (a) and MRI (b)



lateral border of the echogenic area on cUS and the high signal intensity area on MPRAGE images (Fig. 8). The caudate head was measured as the maximum diagonal width from the margin of the lateral ventricle to the outer border of the caudate head, considered to be the outer border of the echolucent area on cUS and the high signal intensity area on MPRAGE images (Fig. 8). The cortex was measured as the depth of the echolucent rim along the cingulate gyrus on cUS and the depth of the high signal intensity line on MPRAGE images (Fig. 7); the echolucent rim and the high signal intensity line are considered to reflect the cortex on, respectively, cUS and MRI. For each anatomical structure, three measurements were performed and, subsequently, the mean was recorded (in millimetres).

Data analysis

All linear measurements on contemporaneous cUS and MRI images were first performed simultaneously to optimize the measuring procedure and to obtain the most accurate comparison of cUS and MRI planes. Subsequently, the measurements on cUS were repeated blinded to the measure from MRI to determine whether there were significant differences between the cUS measurements performed simultaneously with MRI and those performed

blinded. No significant differences or systematic errors ($P>0.05$) were detected between the simultaneous and blinded cUS measurements. The measurements obtained from the MRI were then used as reference values to explore the accuracy of the cUS measurements.

Statistical analyses were performed using StatsDirect statistical software (StatsDirect, Altrincham, UK). In order to explore the accuracy of cUS, as compared to MRI, for linear measurements of different cerebral structures a paired *t*-test and analysis of variances were performed for each parameter. To explore whether there is a correlation between the difference in cUS and MRI measurement and size of the cerebral structure and between the difference in cUS and MRI measurement and various infant growth characteristics, linear regression analyses were performed. The level of significance was taken at 0.05.

Results

Patients

Included in the study were 26 preterm infants (13 male) and 8 term-born infants (all male) who had a cUS and MRI examination on the same day. Mean gestational age (GA)

Fig. 4 Measurement of the VI in the mid-coronal plane (*line*) on cUS (a) and MRI (b)

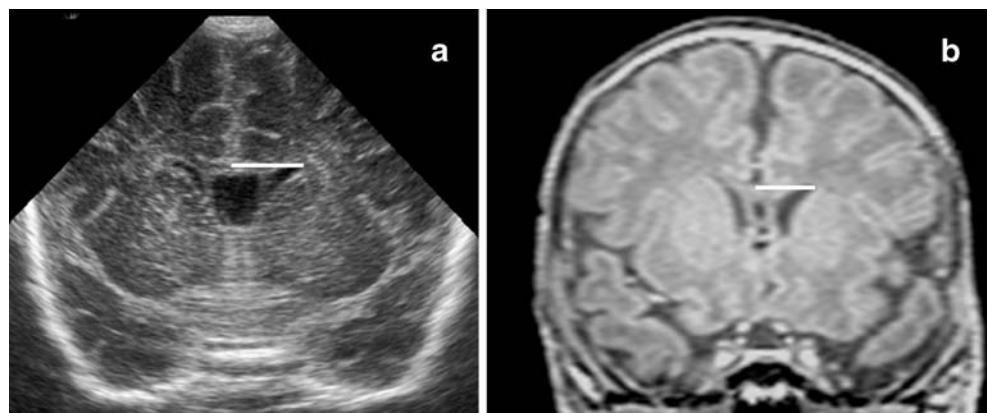
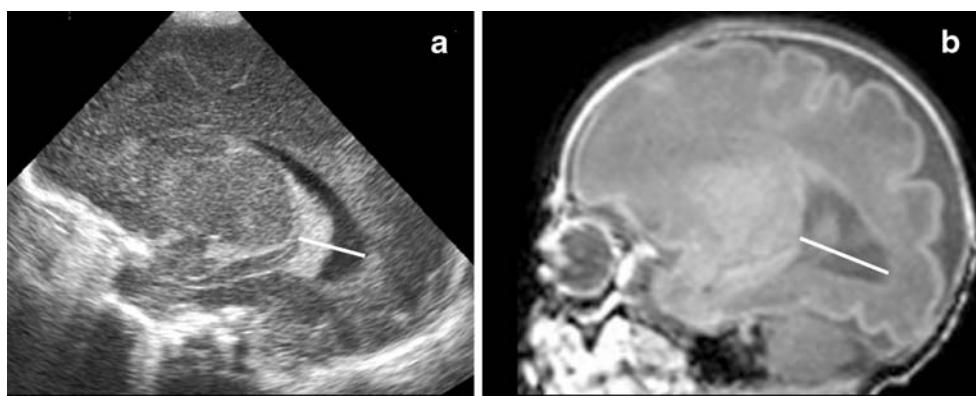


Fig. 5 Measurement of the depth (thalamo-occipital distance) of the posterior horn of the lateral ventricle in a parasagittal plane (*line*) on cUS (a) and MRI (b)



and birth weight were, respectively, 29.5 weeks (range 24.4–32.7 weeks) and 1,230 g (range 586–1,848 g) for preterm infants and 39.4 weeks (38.0–40.6 weeks) and 3,218 g (2,986–3,400 g) for term-born infants. None had major pathology on the cUS or MRI examination. In 9 of the 26 preterm infants and 1 of the 8 term infants, two cUS and MRI examinations were performed on different days. The mean time interval between scans was 7.4 weeks (range 3.7–14.9 weeks). In total, 44 sets of examinations were analysed. Mean corrected GA (CGA) and weight on the day of scanning were, respectively, 37.5 weeks (range 27.1–57.0 weeks) and 2,296 g (range 870–4,210 g) for preterm infants and 42.9 weeks (38.9–49.0 weeks) and 4,007 g (3,127–5,450 g) for term-born infants.

cUS measurements and difference between cUS and MRI

The mean cUS measurements and the differences between the cUS and MRI measurements for the different cerebral structures are shown in Table 1. Significant differences between the cUS and MRI measurements ($P < 0.05$) were found for the VI (left and right), the depth of the posterior horn of the lateral ventricle (left and right), the width of the IHF, the height of the ECS and the depth of the cortex along the cingulate gyrus. For all other measurements the P -value for the differences between the cUS and MRI measurements was > 0.05 . No difference in accuracy of the

cUS measurements or the MRI measurements was found between the preterm and term-born infants. All cUS measurements of the different cerebral structures were appropriate for CGA on the day of scanning, as compared with reference values reported in the literature.

Difference in cUS and MRI measurement and size of cerebral structure

No significant positive or negative correlation was found between the differences in cUS and MRI measurements and size of the measured cerebral structure.

Difference in cUS and MRI measurement and infant growth characteristics

No significant positive or negative correlation was found between the differences in cUS and MRI measurements and GA, weight and head circumference at birth and CGA, weight and head circumference at day of scanning for any infant.

Discussion

Our study showed that linear measurements made from cUS are accurate as compared with measurements made from MR images for most cerebral structures and thus cUS can be

Fig. 6 Measurements of the height and width of the cavum septum pellucidum (*thin lines*) and width of the IHF and height of the ECS (*thick lines*) in the mid-coronal plane on cUS (a) and MRI (b)

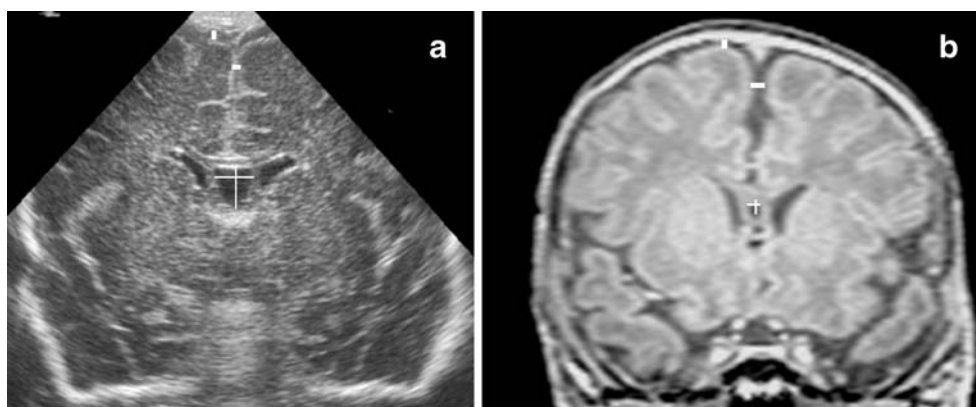
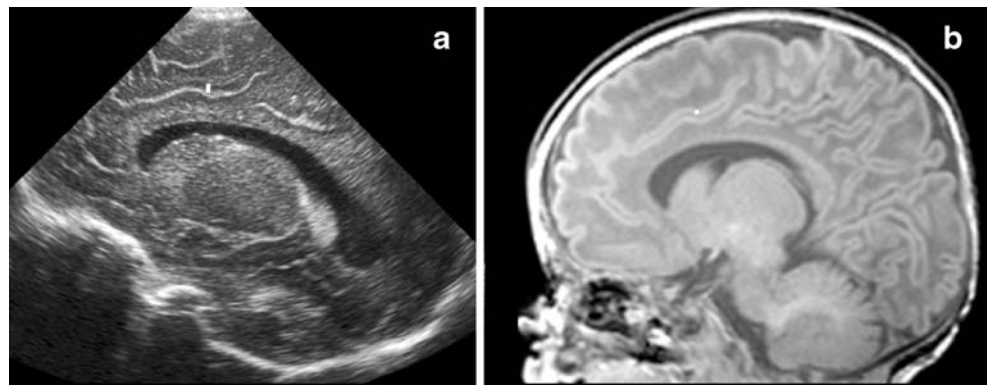


Fig. 7 Measurement of the depth of the cortex along the cingulate gyrus in a parasagittal plane (*line*) on cUS (a) and MRI (b)



reliably used for this purpose. Measurements of the size of the lateral ventricles, including the VI and the depth of the posterior horn, the height of the ECS, the width of the IHF and the depth of the cortex were significantly different from those made using MRI but the absolute differences were unlikely to be of clinical importance. The difference in cortical depth was consistent and more marked but so far this measure on cUS has not been used in a clinical context.

No significant differences in accuracy of the cUS measurements were found between preterm and term-born infants or in relation to their growth characteristics. All our cUS measurements were consistent with reference values in the literature [6, 8, 9, 11–25, 27]. Our study infants were heterogeneous with respect to GA at birth and CGA at scanning and the number of infants was relatively small, so our measurements cannot be used as normative reference values.

The inconsistency between cUS and MRI for measuring the lateral ventricles and the cortical depth was unexpected as these measurements appeared to be easy to make on both cUS and MRI. The difference in measurements of the ECS and IHF were less unexpected as the landmarks are more variable.

The VI of the lateral ventricles [6] measured on cUS is used to diagnose ventriculomegaly and to monitor ventricular size. By comparing measurements of the VI with

expert clinical judgement of ventricular size in preterm infants with normal or mild to severely dilated lateral ventricles, Grasby et al. [32] showed that the VI correlates poorly with clinical judgement and has a low sensitivity for mild dilatation. The measurements of the ventricular height in a parasagittal plane, as described by London et al. [33], and the diagonal width of the frontal horns in a coronal plane, as described by Morony et al. [34], correlate well with expert judgement [32], probably because ballooning of the ventricles is an early sign of dilatation that is not identified by the VI. In addition, Horsch et al. [26] have shown that the ventricular height and frontal horn measurements on cUS correlate well with ventricular volume measurements on MRI. These measurements may therefore be more appropriate for assessing ventricular dilatation than the VI.

The depth of the posterior horn of the lateral ventricle has been suggested as a valuable alternative to the VI, especially as the posterior horn is the first to enlarge in posthaemorrhagic ventricular dilatation [35, 36] and usually the part of the ventricle most dilated antenatally. Consistent with the findings of Horsch et al. [26], we found a significant though small difference between cUS and MRI in measurements of the posterior horn of the lateral ventricles from the back of the thalamus to the furthest point of the occipital horn in an oblique parasagittal plane.

Fig. 8 Measurements of the maximum transverse width of the basal ganglia (*long line*) and the maximum diagonal width of the caudate head (*short line*) in the mid-coronal plane on cUS (a) and MRI (b)

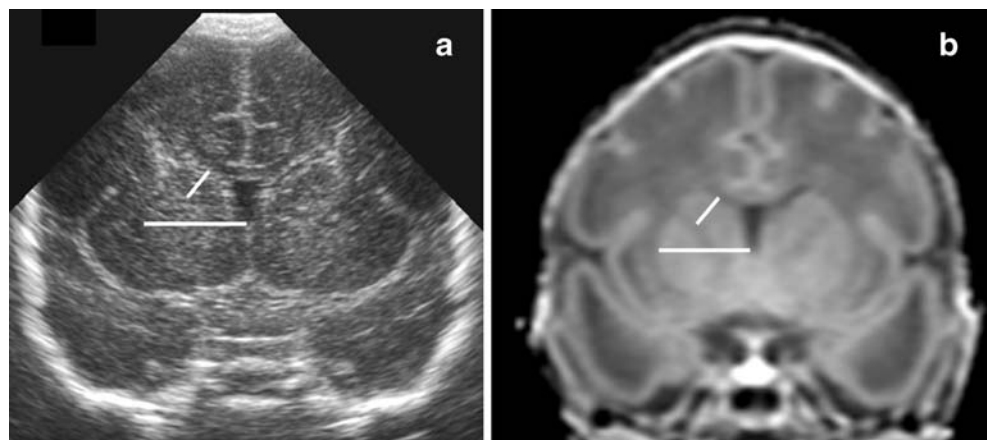


Table 1 Mean cUS measurements and accuracy of cUS measurements as compared to MRI measurements

Cerebral structure		cUS measurement (mm, mean±SD)	Absolute difference, cUS–MRI (mm, mean)	P-value	
				Paired <i>t</i> -test	Analysis of variance
Corpus callosum	Genu	4.21±0.83	0.04	0.569	0.818
	Body	2.40±0.42	0.00	>0.999	>0.999
	Splenium	3.84±0.66	0.07	0.274	0.383
	Length	44.50±4.76	0.20	0.236	0.840
Cerebellum	Height	23.98±5.60	0.08	0.279	0.946
	AP	16.68±3.15	0.01	0.446	0.982
	Width	49.60±8.47	0.28	0.281	0.864
Pons	AP width	14.94±1.96	0.13	0.201	0.604
VI	Left	10.7±2.58	0.54	0.012*	0.569
	Right	10.4±2.39	0.48	0.022*	0.339
Thalamo-occipital distance	Left	19.32±4.36	1.26	0.019*	0.216
	Right	17.48±3.91	1.35	0.007*	0.458
CSP	Height	5.29±2.09	0.18	0.077	0.475
	Width	3.82±1.40	0.07	0.069	0.821
Fourth ventricle	AP width	4.99±1.19	0.14	0.081	0.614
IHF		7.99±4.86	0.31	0.003*	0.821
ECS		4.96±1.98	0.27	0.007*	0.783
Cortical depth		2.00±0.28	0.69	<0.0001*	<0.0001*
Basal ganglia width	Left	19.33±2.43	0.60	0.149	0.271
	Right	19.63±2.24	0.59	0.132	0.273
Caudate head width	Left	4.95±0.61	0.02	0.634	0.885
	Right	4.86±0.57	0.05	0.282	0.723

**P*<0.05

The posterior horn was often difficult to visualize on MRI because of partial volume effects, and on MRI an oblique parasagittal plane is usually not obtained and is difficult to reconstruct; consequently, the full length of the posterior horn was difficult to measure. The apparent poor accuracy of cUS may partly have been due to the inaccuracy of the MRI measurements.

The inaccuracy of cUS for measuring the ECS and IHF is less surprising. Widening of the subarachnoid spaces (including ECS and IHF) can lead to difficulty in interpretation; it may be an indicator of cerebral pathology (e.g. atrophy), potential pathology (e.g. external hydrocephalus), or a normal developmental variant. Horsch et al. [4] have shown that preterm infants with signs of brain atrophy, including widening of the IHF, on cUS at discharge have a poorer neurodevelopmental outcome at 3 years of age. This makes accurate measurements of the ECS and IHF all the more important. We frequently encountered difficulties with cUS measurements of the ECS, mainly caused by loss of signal and presence of artefacts close to the transducer. Govaert et al. [7] used a higher frequency (10 MHz) and Libicher and Troger [9] magnified their cUS images to overcome this difficulty. We were also able to overcome this difficulty by using a higher frequency probe, and

suggest using higher scanning frequencies when performing measurements of the ECS and IHF.

The measurements of the cortical depth on cUS were significantly and consistently greater than on MRI, despite the fact that the cortex seemed relatively easy to define on both cUS and MRI at the site we chose (Fig. 7). MRI studies on cortical depth have shown regional variation in preterm and very-low-birth-weight infants [37]. In addition, cortical surface area and volume are smaller in these infants than in term infants and associated with suboptimal neurodevelopment [37, 38]. Although the medial margin of the cortex, the echolucent rim, mostly appears to be clear on cUS, the subplate and possibly part the subcortical white matter may not be distinguished from the cortex (personal observation). Measuring the cortical depth on MRI has proven difficult and time-consuming [39, 40], and no easy and accurate method has been described. Measurements on MRI may also underestimate the cortical depth.

A possible explanation for the inconsistency between cUS and MRI measurements found in our study may be that cUS and MRI images are obtained at different angles and, consequently, identical planes cannot be obtained. On cUS coronal and sagittal images are obtained through the anterior fontanel angling out from the midline, whereas on MRI

images are obtained in parallel horizontal and vertical planes. Most measurements were performed in the mid-sagittal and mid-coronal plane and MR images were reconstructed to obtain planes that closely resembled the cUS planes. A difference in angle could explain the inconsistency between measurements obtained in parasagittal planes, particularly the posterior horn depth. It could also explain the (non-significant) inconsistency between measurements of cerebral structures with an ovoid shape, such as the lateral ventricles, basal ganglia and caudate heads, or measurements with an ovoid structure as anatomical landmark, such as the thalamus for the measurement of the posterior horn depth. The ovoid shape of several cerebral structures is an intrinsic limit to complete reproducibility of the measurements of these structures.

Inconsistencies in ventricular measurements might result from differences in head position, inducing a shift of cerebrospinal fluid between ventricles. However, Davies et al. have showed that head position has no effect on the size of the lateral ventricles [13]. Therefore, this is an unlikely explanation for the inconsistency between ventricular measurements, but might partly account for differences in ECS measurements.

cUS and MRI are based on completely different methodologies and, consequently, the intrinsic contrast resolution of both techniques is completely different. This may account for some difference in the appearance of anatomical landmarks used for the measurements and difficulties in precisely defining the landmarks, particularly for the measurements of the cortical depth, ventricular width, height of the ECS and width of the IHF. To explore this, histological correlates would be necessary.

For several measurements, including the width of the basal ganglia and the diagonal width of the caudate heads, no reference values have, as yet, been reported. Atrophy of the deep grey matter occurs secondary to basal ganglia and/or white matter damage and is associated with neurodevelopmental delay and is thus of clinical importance. Although the basal ganglia and caudate heads are ovoid structures and therefore reproducible measurements may be more difficult, our experience was that the margins of these structures were not difficult to define visually either with cUS or MRI and that cUS was reliable compared to MRI for measuring the width of the basal ganglia and caudate heads, and we suggest that cUS can be used for early detection of deep grey-matter atrophy.

Anderson et al. [28] have suggested that measurements performed on cUS are limited in reflecting variations in cerebral structure. However, they compared and correlated linear measurements on two-dimensional cUS with volume measurements on three-dimensional MRI, which is difficult for various practical and technical reasons. In addition, they compared cUS and MRI examinations that were performed with a median time interval of 4 days (range 0–28 days)

between scans, which might partly have caused the poor correlation between cUS and MRI for several measurements.

Limitations of our study were that sometimes exactly the same planes could not be compared and that the methodologies of the two imaging tools are different, making direct correlation of cUS and MRI for several measurements difficult. Secondly, we had no direct histological correlates and MRI measurements were used to explore the accuracy of cUS. However, we believe that as the MRI measurements were consistent with reference values in the literature, correlating cUS measurements with MRI measurements is valid for most cerebral structures. We did not perform cUS using a higher frequency in all infants, which might have overcome the limited accuracy of cUS in measuring the ECS. Finally, we did not include infants with major pathology, and it is important to determine that the consistency in measurements holds true when structures are abnormal. We have compared cUS and MRI measurements in eight infants, not included in this study, with hypoxic-ischemic encephalopathy associated with moderate cerebral abnormalities and found cUS to have an accuracy similar to that in infants with a normal brain.

Conclusion

Although more work is needed to optimize the linear measurements for which a limited accuracy of cUS was found, and reference values for several cerebral structures have, as yet, not been established, we found cUS a reliable tool for measuring most clinically important structures in the newborn infant brain. Not only is this useful for diagnosis of more major cerebral developmental abnormalities but it also allows the bedside assessment of more subtle alterations in growth that affect the preterm infant brain.

Acknowledgements This research was undertaken with financial support from The Doctor Catharina van Tussenbroek Foundation, The Academy of Medical Science, The Health Foundation, Philips Medical Systems, and the March of Dimes Foundation.

References

1. Cooke RW, Abernethy LJ (1999) Cranial magnetic resonance imaging and school performance in very low birth weight infants in adolescence. *Arch Dis Child* 81:F116–F121
2. Peterson BS, Vohr B, Staib LH et al (2000) Regional brain volume abnormalities and long-term cognitive outcome in preterm infants. *JAMA* 284:1939–1947
3. Inder TE, Warfield SK, Wang H et al (2005) Abnormal cerebral structure is present at term in premature infants. *Pediatrics* 115:286–294
4. Horsch S, Muentjes C, Franz A et al (2005) Ultrasound diagnosis of brain atrophy is related to neurodevelopmental outcome in preterm infants. *Acta Paediatr* 94:1815–1821

5. Lodygensky GA, Rademaker K, Zimine S et al (2005) Structural and functional brain development after hydrocortisone treatment for neonatal chronic lung disease. *Pediatrics* 116:1–7
6. Levene MI (1981) Measurements of the growth of the lateral ventricles in preterm infants with real-time ultrasound. *Arch Dis Child* 56:900–904
7. Govaert P, Pauwels W, Vanhaesebrouck P et al (1989) Ultrasound measurement of the subarachnoid space in infants. *Eur J Pediatr* 148:412–413
8. Mott SH, Bodensteiner KB, Allan WC (1992) The cavum septi pellucidi in term and preterm newborn infants. *J Child Neurol* 7:35–38
9. Libicher M, Troger J (1992) US measurement of the subarachnoid space in infants: normal values. *Radiology* 184:749–751
10. Iai M, Tanabe Y, Goto M et al (1994) A comparative magnetic resonance imaging study of the corpus callosum in neurologically normal children and children with spastic diplegia. *Acta Paediatr* 83:1086–1090
11. Anderson N, Wells E, Hay R et al (1996) Cerebellar vermis measurement at cranial sonography for assessing gestational age in the newborn weighing less than 2000 grams. *Early Hum Dev* 44:59–70
12. Jou HJ, Shyu MK, Wu SC et al (1998) Ultrasound measurement of the fetal cavum septi pellucidi. *Ultrasound Obstet Gynecol* 12:419–421
13. Davies MW, Swaminathan M, Chuang SL et al (2000) Reference ranges for the linear dimensions of the intracranial ventricles in preterm neonates. *Arch Dis Child* 82:F218–F223
14. Makhoul IR, Goldstein I, Epelman M et al (2000) Neonatal transverse cerebellar diameter in normal and growth-restricted infants. *J Matern Fetal Med* 9:155–160
15. Davies MW, Swaminathan M, Betheras FR (2001) Measurement of the transverse cerebellar diameter in preterm neonates and its use in assessment of gestational age. *Australas Radiol* 45:309–312
16. Achiron R, Achiron A (2001) Development of the human fetal corpus callosum: a high-resolution, cross-sectional sonographic study. *Ultrasound Obstet Gynecol* 18:343–347
17. Lam WW, Ai VH, Wong V et al (2001) Ultrasonographic measurement of subarachnoid space in normal infants and children. *Pediatr Neurol* 25:380–384
18. Malinger G, Ginath S, Lerman-Sagie T et al (2001) The fetal cerebellar vermis: normal development as shown by transvaginal ultrasound. *Prenat Diagn* 21:687–692
19. Goldstein I, Makhoul IR, Tamir A et al (2002) Ultrasonographic nomograms of the fetal fourth ventricle: additional tool for detecting abnormalities of the posterior fossa. *J Ultrasound Med* 21:849–856
20. Zalel Y, Seidman DS, Brandt N et al (2002) The development of the fetal vermis: an in-utero sonographic evaluation. *Ultrasound Obstet Gynecol* 19:136–139
21. Serhatlioglu S, Kocakoc E, Kiris A et al (2003) Sonographic measurement of the fetal cerebellum, cisterna magna, and cavum septum pellucidum in normal fetuses in the second and third trimesters of pregnancy. *J Clin Ultrasound* 31:194–200
22. Achiron R, Kivilevitch Z, Lipitz S et al (2004) Development of the human fetal pons: in utero ultrasonographic study. *Ultrasound Obstet Gynecol* 24:506–510
23. Chavez MR, Ananth CV, Smulian JC et al (2004) Fetal trans-cerebellar diameter measurement with particular emphasis in the third trimester: a reliable predictor of gestational age. *Am J Obstet Gynecol* 191:979–984
24. Triulzi F, Parazzini C, Righini A (2005) MRI of fetal and neonatal cerebellar development. *Semin Fetal Neonatal Med* 10:411–420
25. Anderson NG, Laurent I, Cooke N et al (2005) Growth rate of corpus callosum in very premature infants. *AJNR* 26:2685–2690
26. Horsch S, Bengtsson J, Nordell A et al (2006) Lateral ventricular size in extremely premature infants: 3D MRI confirms 2D ultrasound measurements. Proceedings of the Annual Meeting of the Pediatric Academic Societies, San Francisco, CA
27. Anderson NG, Laurent I, Woodward LJ et al (2006) Detection of impaired growth of the corpus callosum in premature infants. *Pediatrics* 118:951–960
28. Anderson NG, Warfield SK, Wells S et al (2004) A limited range of measures of 2-D ultrasound correlate with 3-D MRI cerebral volumes in the premature infant at term. *Ultrasound Med Biol* 30:11–18
29. Mercuri E, Guzzetta A, Laroche S et al (2003) Neurologic examination of preterm infants at term age: Comparison with term infants. *J Pediatr* 142:647–655
30. Dubowitz L, Ricciw D, Mercuri E (2005) The Dubowitz neurological examination of the full-term newborn. *Ment Retard Dev Disabil Res Rev* 11:52–60
31. Cowan FM (1998) Sedation for magnetic resonance scanning of infants and young children. In: Whitwam JG, McCloy RF (eds) Principles and practice of sedation. Blackwell Healthcare, London, pp 206–213
32. Grasby DC, Esterman A, Marshall P (2003) Ultrasound grading of cerebral ventricular dilatation in preterm infants. *J Paediatr Child Health* 39:186–190
33. London DA, Carroll BA, Enzmann DR (1980) Sonography of ventricular size and germinal matrix hemorrhage in premature infants. *AJNR* 1:295–300
34. Morony S, Marshall P, Langlois S (1984) Periventricular haemorrhage and ventricular dilatation detected by real time ultrasound in infants <1500 g birthweight. *Aust Paediatr J* 20:252
35. Silverboard G, Horder MH, Ahmann PA et al (1980) Reliability of ultrasound diagnosis of intracerebral hemorrhage and posthemorrhagic hydrocephalus: comparison with CT. *Pediatrics* 66:507–514
36. Brann BS, Qualls C, Wells L et al (1991) Asymmetric growth of the lateral cerebral ventricle in infants with posthemorrhagic ventricular dilatation. *J Pediatr* 118:108–112
37. Martinussen M, Fischl B, Larsson HB et al (2005) Cerebral cortex thickness in 15-year-old adolescents with low birth weight measured by an automated MRI-based method. *Brain* 128:2588–2596
38. Ajayi-Obe M, Saeed N, Cowan FM et al (2000) Reduced development of cerebral cortex in extremely preterm infants. *Lancet* 356:1162–1163
39. Fischl B, Dale AM (2000) Measuring the thickness of the human cerebral cortex from magnetic resonance images. *Proc Natl Acad Sci U S A* 97:11050–11055
40. Kabani N, Le Goualher G, MacDonald D et al (2001) Measurement of cortical thickness using an automated 3-D algorithm: a validation study. *Neuroimage* 13:375–380