Ultrasound Obstet Gynecol 2014; **44**: 388–393
Published online 21 August 2014 in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.13429

Additional value of fetal magnetic resonance imaging in the prenatal diagnosis of central nervous system anomalies: a systematic review of the literature

A. C. ROSSI* and F. PREFUMO†

**Department of Obstetrics and Gynaecology, University of Bari, Bari, Italy; †Maternal-Fetal Medicine Unit, Department of Obstetrics and Gynaecology, University of Brescia, Brescia, Italy*

KEYWORDS: central nervous system; fetal malformations; fetal ultrasound; magnetic resonance imaging; prenatal diagnosis

ABSTRACT

Objectives *To analyze literature on the additional value of fetal magnetic resonance imaging (MRI) in assessing central nervous system (CNS) anomalies suspected by ultrasound.*

Methods *A search was performed of PubMed, EMBASE, Cochrane library and the reference lists of identified articles. Inclusion criteria were CNS anomalies suspected/diagnosed by ultrasound, MRI performed after ultrasound, and postmortem examination by autopsy or postnatal assessment. MOOSE guidelines were followed. Outcomes assessed were positive/negative agreement between ultrasound and MRI, additional information provided by MRI, and discordance between ultrasound and MRI. Pooled sensitivity and specificity of MRI were calculated using the DerSimonian–Laird method. Postnatal/postmortem examinations were used as the reference standard.*

Results *We identified thirteen articles which included 710 fetuses undergoing both ultrasound and MRI. MRI confirmed ultrasound-positive findings in 65.4% of fetuses and provided additional information in 22.1%. MRI disclosed CNS anomalies in 18.4% of fetuses. In 2.0% of cases, ultrasound was more accurate than MRI. In 30% of fetuses, MRI was so different from ultrasound that the clinical management changed. Agreement was observed mainly for ventriculomegaly (51.3%). Disagreement was noted mainly for midline anomalies (48.6%). Pooled sensitivity of MRI was 97% (95% CI, 95–98%) and pooled specificity was 70% (95% CI, 58–81%).*

Conclusions *MRI supplements the information provided by ultrasound. It should be considered in selected fetuses with CNS anomalies suspected on ultrasound.* *Copyright © 2014 ISUOG. Published by John Wiley & Sons Ltd.*

INTRODUCTION

Ultrasound is the primary imaging technique for the assessment of fetal brain anatomy. The acquisition of high-resolution images, the real-time imaging and the relatively low cost are some advantages of ultrasound. Limitations of neurosonography are largely secondary to reverberation artifacts of the bony calvarium, beam attenuation by adipose tissue, oligohydramnios, fetal engagement in the maternal pelvis and a low sensitivity to detect malformations of cerebral cortical development. Because of these disadvantages, some fetuses with anomalies cannot be evaluated adequately by ultrasound and require additional information for management and counseling.

Fetal magnetic resonance imaging (MRI) was first described in the 1990s, but image degradation by fetal motion and the relatively long acquisition time discouraged the use of MRI for the examination of fetal anatomy[1]. The use of MRI was successively re-evaluated with the introduction of ultrafast techniques, which minimized fetal movement artifacts and improved visualization of fetal images[2]. The superiority of MRI over ultrasound has been questioned, in particular with regard to the diagnosis of migration disorders, callosal anomalies and pathologies of the posterior fossa[3–5]. In a study that compared MRI and ultrasound, the two modalities were statistically similar[6].

Fetal MRI is generally indicated when fetal ultrasound is suspicious or the sonographic detection of fetal malformations requires further assessment. Because fetal MRI is not performed in cases of negative ultrasound, studies on fetal MRI are unable to assess true-negative and false-negative cases, making sensitivity, specificity and predictive values questionable. Nonetheless, knowledge of if and how fetal MRI improves the prenatal diagnosis of cerebral malformations in contemporary practice might be useful.

Correspondence to: Dr F. Prefumo, Maternal-Fetal Medicine Unit, Department of Obstetrics and Gynaecology, University of Brescia, Piazzale Spedali Civili, 1, 25123 Brescia, Italy (e-mail: federico.prefumo@gmail.com)

Accepted: 23 May 2014

The aim of this review was to evaluate the additional value of fetal MRI in the detection of central nervous system (CNS) anomalies suspected by ultrasound.

METHODS

A search was performed in PubMed, EMBASE, Medline and reference lists to find articles published from January 2000 to December 2012 that compared ultrasound and MRI for detection of CNS anomalies. The search was limited to articles published no earlier than 2000 because improvements in both MRI and fetal neurosonography techniques have made their diagnostic accuracy higher than earlier experiences in either field. Keywords were: CNS anomalies/malformations; prenatal ultrasound; fetal magnetic resonance (imaging); fetal brain; and prenatal diagnosis.

Inclusion criteria for study selection were: CNS anomalies suspected or diagnosed by ultrasound; fetal MRI performed after ultrasound; and postmortem examination by autopsy or postnatal neurologic assessment by ultrasound, MRI or clinical examination. Exclusion criteria were: omission of at least one inclusion criterion; data reported in graphs or as percentages; and/or non-English language publication. From each article, data abstracted were: gestational age at time of MRI; type of CNS anomaly; ultrasound findings; MRI findings; and postnatal/postmortem findings.

Outcomes of interest were:

- positive agreement between ultrasound and MRI findings: both methods identify fetal abnormalities;
- negative agreement between ultrasound and MRI findings: both methods do not identify fetal abnormalities;
- information provided by MRI additional to ultrasound findings: both methods identify fetal abnormalities, but MRI detects additional anomalies;
- discordance between ultrasound and MRI images: ultrasound identifies fetal abnormalities that are not confirmed by MRI, or ultrasound does not identify fetal abnormalities that are identified by MRI.

Postnatal/postmortem findings were used as the reference standard.

Types of CNS anomalies were grouped as follows: ventriculomegaly; midline anomalies (holoprosencephaly, cranioschisis, corpus callosum agenesis/lipoma, Chiari II malformation, Dandy–Walker malformation/variant); neuronal migration anomalies (lissencephaly, megalencephaly, schizencephaly, arachnoid cyst, glioependymal cyst, choroid plexus cyst), hemorrhage (porencephaly, hydranencephaly); vascular defects (vein of Galen aneurysm, arteriovenous fistula); and neural cell proliferation disorders (microcephaly, macrocephaly, tumors).

Study selection and data extraction were performed independently by the authors according to the Meta-Analyses Of Observational Studies in Epidemiology (MOOSE) guidelines. The two authors independently selected articles and abstracted data. Discordance was resolved with consensus.

The Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) was used to assess the quality of the studies included in the analysis[7]. QUADAS-2 is a tool used to evaluate the risk of bias and applicability of primary diagnostic accuracy studies. It is composed of four domains: patient selection; index test; reference standard; and flow and timing. For each domain, the risk of bias is assessed as 'low', 'high' or 'unclear'. For the first three domains, the applicability is also assessed[8,9].

Pooled sensitivity and specificity of fetal MRI were calculated using the DerSimonian–Laird method. Receiver–operating characteristics (ROC) curves were plotted and the area under the curve (AUC) was calculated. Analyses were performed using MetaDisc 1.3[10].

RESULTS

Steps for study selection are reported in Figure S1 and characteristics of each study are reported in Table S1. Of 30 articles selected for detailed evaluation, 17 were excluded because they did not completely fulfill inclusion criteria; a list of these articles with reasons for exclusion is provided in Table S2. Thirteen articles were therefore included in the analysis, with a total of 710 fetuses undergoing both ultrasound and MRI[5,11–22].

The QUADAS-2 assessment (Figure 1) demonstrates that only three of 13 studies had a low risk of bias regarding patient selection. This is explained by the fact that many studies did not define criteria for offering MRI, limited MRI to 'difficult' or 'selected' cases, were retrospective or did not include consecutive cases; furthermore, only four studies provided details on the protocol used for ultrasound examination. In 10/13 studies the protocol for MRI examination and its timing in relation to ultrasound were clearly defined, leading to a low risk of bias in the index test domain. In most studies (11/13) the reference standard was fully consistent with the inclusion criteria for our review (postmortem examination by autopsy or postnatal neurologic assessment by ultrasound, MRI or clinical examination). Finally, 10/13 had a low risk of bias in the flow and timing domain, as they gave sufficient details on follow up and exclusions. The applicability was generally satisfactory in the index test and reference standard domains. As for patient selection, there was concern regarding applicability in five of 13 studies, given the aforementioned limitations in design.

Gestational age at the time of MRI ranged widely, from 16 to 39 weeks[20]. MRI confirmed ultrasound findings in 464 (65.4%) fetuses and provided additional information in 157 (22.1%). In 40 (5.6%) fetuses, ultrasound revealed CNS anomalies that were not shown by MRI, but the abnormalities were confirmed at postnatal/postmortem examination in only nine. The remaining 49 (6.9%) fetuses underwent MRI in spite of negative brain ultrasound because of cytomegalovirus (CMV) infection,

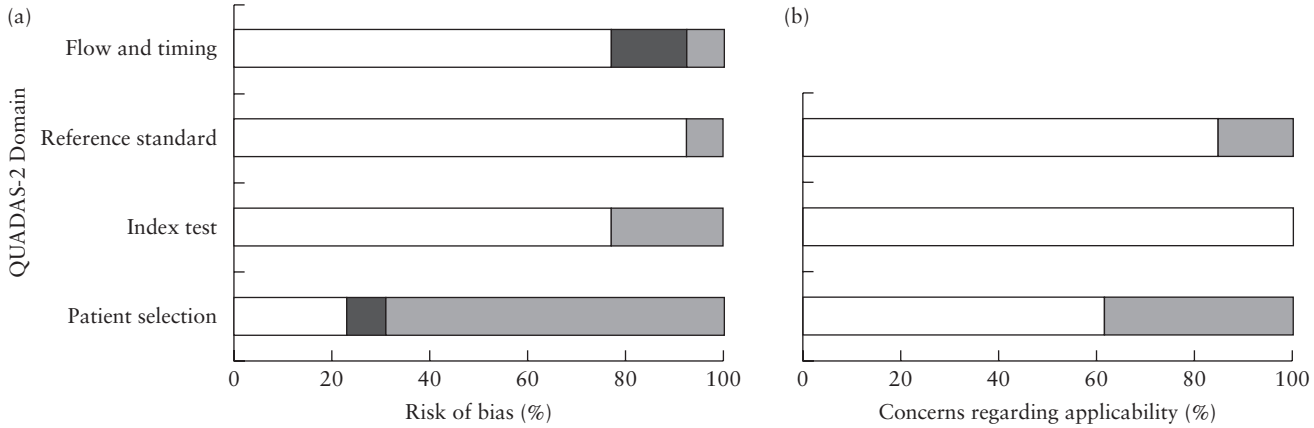

Figure 1 Quality assessment of studies included in this review, using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool. Proportions of studies with low (□), high (■) or unclear (▩) risk of bias (a) or concerns regarding applicability (b) are shown.

non-CNS ultrasound anomalies or cotwin anomalies. MRI confirmed negative findings in 40 (81.6%) of these fetuses and disclosed CNS anomalies in nine (18.4%). From three articles, it was specified that in 65 (30.2%) of 215 fetuses, prenatal MRI was so markedly different from ultrasound that the clinical management of these pregnancies drastically changed according to MRI findings.

In 405 (57.0%) fetuses, the type of anomaly was described. Abnormalities consisted of midline anomalies ($n = 137$; 33.8%), ventriculomegaly ($n = 181$; 44.7%), hemorrhage ($n = 29$; 7.2%), neuronal migration disorders ($n = 23$; 5.7%), nerve cell proliferation disorders ($n = 12$; 3.0%), vascular defects ($n = 8$; 2.0%) and multiple anomalies ($n = 15$; 3.7%). The highest rate of agreement (both ultrasound-positive and MRI-positive) was observed in the detection of ventriculomegaly (51.3%). In 93 fetuses, ventriculomegaly was isolated according to ultrasound, but MRI disclosed further anomalies, mainly hemorrhage (nine cases) and corpus callosum agenesis (nine cases). Disagreement was noted mainly with regard to midline anomalies (48.6% for ultrasound-positive and MRI-negative and 40.5% for ultrasound-negative and MRI-positive) (Figure 2).

Postnatal/postmortem examination confirmed prenatal MRI findings in 630 (88.7%) cases and provided additional information in nine (1.3%). In 18 (2.5%) cases, postnatal/postmortem examination was negative, in contrast to prenatal MRI. This over-diagnosis by MRI consisted of ventriculomegaly in six (33.3%) cases, hemorrhage in six (33.3%), midline anomalies in three (16.7%), neuronal migration anomalies in two (11.1%) and nerve cell proliferation disorders in one (5.5%). There were 40 (5.6%) cases in which both prenatal MRI and postnatal/postmortem examination were negative. In the remaining 13 (1.8%) cases, postnatal examination diagnosed CNS anomalies that were missed by prenatal MRI. These included five (38.4%) cases of midline anomalies, four (30.7%) of ventriculomegaly, three (23.0%) of nerve cell proliferation disorders and one (7.7%) of vascular defect.

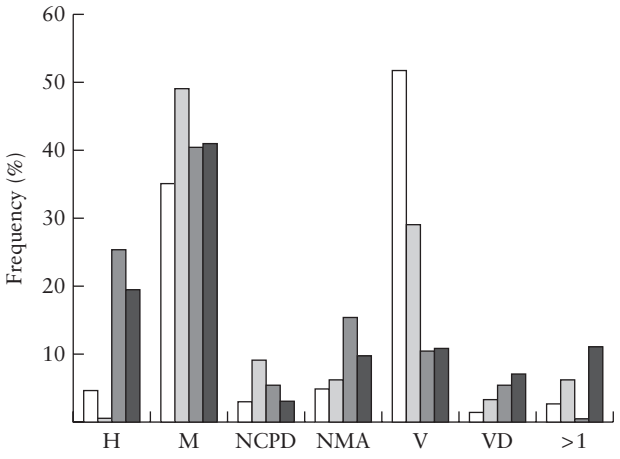

Figure 2 Rates of agreement and disagreement between prenatal ultrasound (US) and magnetic resonance imaging (MRI). Histograms show the contribution (%) of each abnormality type to the following diagnostic categories: □, US+/MRI+ (positive agreement between ultrasound and MRI findings; both methods identify fetal abnormalities); ▨, US+/MRI− (abnormality seen on ultrasound, not confirmed by MRI); ▩, US−/MRI+ (abnormality not suspected on ultrasound, diagnosed by MRI); and ■, additional information (both ultrasound and MRI identify fetal abnormality, but MRI detects additional features). > 1, more than one anomaly; H, hemorrhage; M, midline anomalies; NCPD, neural cell proliferation disorders; NMA, neuronal migration anomalies; V, ventriculomegaly; VD, vascular disease.

Pooled sensitivity and specificity are reported in Figure 3. The AUC was 0.86 (95% CI, 0.77–0.95; Figure 4).

In 14 (2.0%) cases, ultrasound was more accurate than MRI. In particular, there were nine cases in which MRI did not detect CNS anomalies (one of nerve cell proliferation, two of ventriculomegaly, one of hemorrhage, two of neuronal migration anomalies and three of midline anomalies), three cases in which MRI, but not ultrasound, revealed CNS anomalies that were not detected at birth (two nerve cell proliferation disorders and one hemorrhage) and two cases with discordant abnormal diagnosis (one of hemorrhage by MRI and ventriculomegaly by ultrasound and

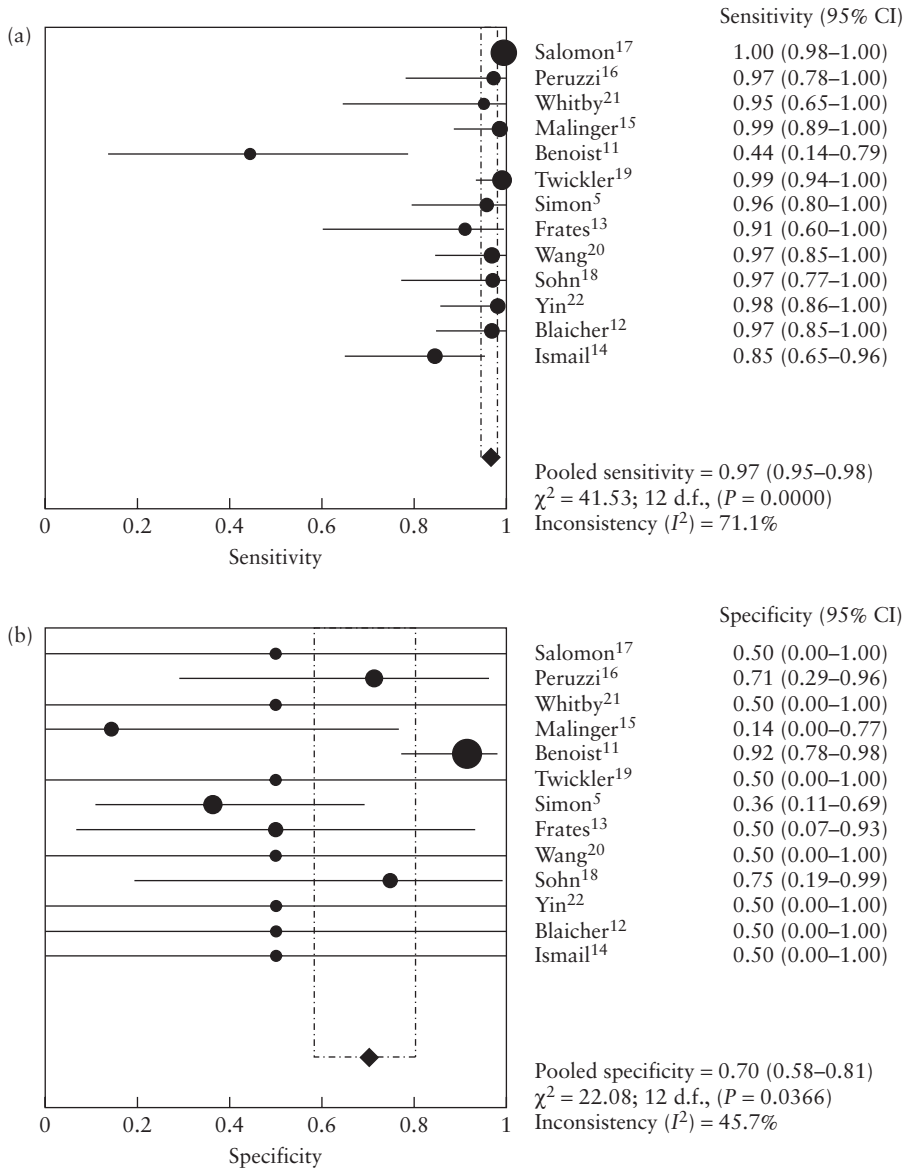

Figure 3 Pooled sensitivity (a) and pooled specificity (b) of fetal magnetic resonance imaging in the diagnosis of central nervous system anomalies. The size of the data points is proportional to number of fetuses. Only the first author of each study is given.

one of ventriculomegaly by MRI and calcifications by ultrasound). In all these cases, postnatal findings confirmed the prenatal ultrasound diagnosis.

DISCUSSION

This review shows that there is approximately 65% agreement between ultrasound and MRI in detecting CNS anomalies, and the highest agreement was noted for ventriculomegaly. MRI provided additional information in 22% of cases, mainly in those with midline anomalies. This finding suggests that MRI may be considered when midline malformations are detected by ultrasound. In spite of the high agreement with regard to negative findings at both ultrasound and MRI (82%), it should be highlighted that in 18% of cases, MRI detected CNS anomalies that were missed by ultrasound. Another important finding of our review was that in 30% of cases, the ultrasound diagnosis was so revised by MRI that management and parental counseling changed completely. However, MRI is not error-free. Our review found that in a minority of cases, postnatal examination revealed CNS anomalies that were not diagnosed by MRI (2%) and other cases in which ultrasound was superior to MRI (2%). In addition, false-positive MRI images were detected in 2.5% of fetuses. Midline anomalies represented the highest reason for disagreement. This could be explained by the fact that midline anomalies include posterior fossa anomalies and absence of the corpus callosum, which are better imaged on sagittal views than on routine axial views on ultrasound. It is possible that ultrasound scans may not have included a midline sagittal view, obtained either transabdominally or transvaginally, owing to an unfavorable fetal position or insufficient operator training. Only four studies provided details on the protocol used for ultrasound examinations;

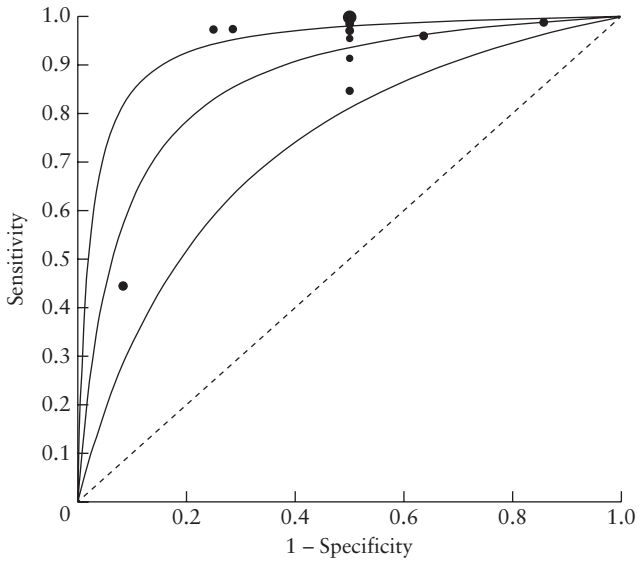

Figure 4 Summary receiver–operating characteristics curve with 95% CIs. Area under the curve ± SE = 0.861 ± 0.047; Q* ± SE = 0.792 ± 0.046. The size of the data points is proportional to number of fetuses.

however, these all included at least direct visualization of the corpus callosum. It is therefore impossible to determine to what extent the additional value of MRI, found in our review for midline anomalies, is intrinsic to the MRI approach or may be reduced by improvements in ultrasound techniques.

It may be argued that the high accuracy of MRI depends on the fact that radiologists are aware of patients' history and ultrasound findings, whereas ultrasound is performed on unselected populations as a screening test. However, in the present review, almost all fetuses were managed in tertiary care centers to which they were referred for suspected CNS anomalies. Therefore, sonographers, as well as radiologists, were not blind to potential CNS anomalies.

Prenatal MRI may be particularly useful for anomalies involving cerebral structures that are not easily identifiable by ultrasound. This is the case for abnormalities whose characterization relies on sagittal views, as discussed before. Similarly, neural cysts are better defined by MRI with regard to location, origin and parenchymal compression. Intracranial hemorrhage is another condition for which MRI is additional to ultrasound diagnosis because it documents the extent of the bleeding, involvement of the surrounding tissue and porencephalic cavities of small size.

Other limitations of our review, mainly resulting from lack of information in the original literature, must be pointed out. We could not compare ultrasound and MRI according to gestational age. Twickler *et al.* found that MRI works better than ultrasound at later gestation[19]. A possible explanation could be that fetal motion is reduced in the third trimester and this reduction allows better MRI definition. In addition, fetal head engagement, maturation of the skull bones and reduction of amniotic fluid volume, which occur in the third trimester, decrease the accuracy of ultrasound. Levine *et al.* found that third-trimester fetuses are more likely to have changes in diagnosis, management and parental counseling, compared with second-trimester fetuses[23]. If MRI is performed a long time after ultrasound, this could partly account for an increased detection of abnormalities. Unfortunately, not all studies reported the ultrasound-to-MRI interval; in those that did, it was often less than 1–2 weeks, an interval that should not significantly affect diagnostic accuracy.

We did not stratify severity of ventriculomegaly, or discriminate between unilateral and bilateral ventriculomegaly, but we observed that MRI was useful for disclosing additional anomalies. We found that isolated ventriculomegaly can be associated with sonographically undetected anomalies in approximately 19% of cases. This risk is higher than the risk reported by Solomon *et al.*, who observed that in isolated mild ventriculomegaly there is a 6% risk of associated major anomalies that are missed by ultrasound[17]. Noteworthy, Solomon *et al.* analyzed ventriculomegaly in the third trimester and used an extensive ultrasound protocol, whereas our review included ventriculomegaly detected by ultrasound during the second and third trimesters. In addition, mild ventriculomegaly normalizes in approximately 40% of fetuses[24].

Because only one study included a control group of negative ultrasound undergoing MRI, true-/false-negative cases were not available. Therefore, it was not possible to calculate the agreement between ultrasound and MRI. Moreover, it is very unlikely in prenatal care that women would have MRI in spite of negative ultrasound. Only Benoist *et al.* performed MRI, because of CMV infection, and calculated sensitivity for ultrasound alone (85%), MRI alone (42%) and for the combination of the two techniques (89%)[11]. The low sensitivity in their group was explained by the fact that most CMV-related anomalies manifest as brain calcifications that could be missed prenatally because of their small size. Although it was not possible to calculate the agreement between ultrasound and MRI, we observed that pooled sensitivity of MRI was very high (97%).

It cannot be emphasized enough that both ultrasound and MRI are operator-dependent techniques. Knowledge of normal and pathological fetal neuroanatomy, natural history of abnormalities and clinical judgment are of paramount importance for interpretation of the diagnostic images. Moreover, ultrasound of the fetal brain, whether performed transabdominally or transvaginally, requires appropriate technical skills to obtain the correct diagnostic images[25]. Therefore, local conditions and expertise in individual centers may greatly affect the accuracy of these diagnostic modalities.

In conclusion, MRI is a non-invasive technique that supplements the information provided by ultrasound because it allows precise visualization and determination of the extent and severity of anomalies and of the presence of associated anomalies in a subgroup of

fetuses with sonographically suspected or diagnosed CNS malformations. Because this additional information may change radically management of the pregnancy, MRI should be considered in selected fetuses with CNS anomalies suspected on ultrasound.

REFERENCES

1. Yuh WT, Nguyen HD, Fisher DJ, Tali ET, Gao F, Simonson TM, Kao SC, Weiner CP. MR of fetal central nervous system abnormalities. *AJNR Am J Neuroradiol* 1994; **15:** 459–464.
2. Levine D, Barnes PD, Sher S, Semelka RC, Li W, McArdle CR, Worawattanakul S, Edelman RR. Fetal fast MR imaging: reproducibility, technical quality, and conspicuity of anatomy. *Radiology* 1998; **206:** 549–554.
3. Girard N, Raybaud C, Gambarelli D, Figarella-Branger D. Fetal brain MR imaging. *Magn Reson Imaging Clin N Am* 2001; **9:** 19–56, vii.
4. Levine D, Barnes PD, Madsen JR, Abbott J, Mehta T, Edelman RR. Central nervous system abnormalities assessed with prenatal magnetic resonance imaging. *Obstet Gynecol* 1999; **94:** 1011–1019.
5. Simon EM, Goldstein RB, Coakley FV, Filly RA, Broderick KC, Musci TJ, Barkovich AJ. Fast MR imaging of fetal CNS anomalies in utero. *AJNR Am J Neuroradiol* 2000; **21:** 1688–1698.
6. Kubik-Huch RA, Huisman TA, Wisser J, Gottstein-Aalame N, Debatin JF, Seifert B, Ladd ME, Stallmach T, Marincek B. Ultrafast MR imaging of the fetus. *AJR Am J Roentgenol* 2000; **174:** 1599–1606.
7. University of Bristol. QUADAS-2. http://www.bris.ac.uk/quadas/ [Accessed 10 November 2013].
8. Whiting P, Rutjes AW, Reitsma JB, Bossuyt PM, Kleijnen J. The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC Med Res Methodol* 2003; **3:** 25.
9. Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, Leeflang MM, Sterne JA, Bossuyt PM, Group Q-. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011; **155:** 529–536.
10. Zamora J, Abraira V, Muriel A, Khan KS, Coomarasamy A. Meta-DiSc: a software for meta-analysis of test accuracy data. *BMC Med Res Methodol* 2006, **6**: 31. www.hrc.es/investigacion/metadisc_en.htm [Accessed 9 September 2013].
11. Benoist G, Salomon LJ, Mohlo M, Suarez B, Jacquemard F, Ville Y. Cytomegalovirus-related fetal brain lesions: comparison between targeted ultrasound examination and magnetic resonance imaging. *Ultrasound Obstet Gynecol* 2008; **32:** 900–905.
12. Blaicher W, Prayer D, Mittermayer C, Weninger M, Birnbacher R, Deutinger J, Bernaschek G. The clinical impact of magnetic resonance imaging in fetuses with central nervous system anomalies on ultrasound scan. *Ultraschall Med* 2005; **26:** 29–35.
13. Frates MC, Kumar AJ, Benson CB, Ward VL, Tempany CM. Fetal anomalies: comparison of MR imaging and ultrasound for diagnosis. *Radiology* 2004; **232:** 398–404.
14. Ismail KM, Ashworth JR, Martin WL, Chapman S, McHugo J, Whittle MJ, Kilby MD. Fetal magnetic resonance imaging in prenatal diagnosis of central nervous system abnormalities: 3-year experience. *J Matern Fetal Neonatal Med* 2002; **12:** 185–190.
15. Malinger G, Ben-Sira L, Lev D, Ben-Aroya Z, Kidron D, Lerman-Sagie T. Fetal brain imaging: a comparison between magnetic resonance imaging and dedicated neurosonography. *Ultrasound Obstet Gynecol* 2004; **23:** 333–340.
16. Peruzzi P, Corbitt RJ, Raffel C. Magnetic resonance imaging versus ultrasonography for the in utero evaluation of central nervous system anomalies. *J Neurosurg Pediatr* 2010; **6:** 340–345.
17. Salomon LJ, Ouahba J, Delezoide AL, Vuillard E, Oury JF, Sebag G, Garel C. Third-trimester fetal MRI in isolated 10- to 12-mm ventriculomegaly: is it worth it? *BJOG* 2006; **113:** 942–947.
18. Sohn YS, Kim MJ, Kwon JY, Kim YH, Park YW. The usefulness of fetal MRI for prenatal diagnosis. *Yonsei Med J* 2007; **48:** 671–677.
19. Twickler DM, Magee KP, Caire J, Zaretsky M, Fleckenstein JL, Ramus RM. Second-opinion magnetic resonance imaging for suspected fetal central nervous system abnormalities. *Am J Obstet Gynecol* 2003; **188:** 492–496.
20. Wang GB, Shan RQ, Ma YX, Shi H, Chen LG, Liu W, Qiu XL, Wei YL, Guo L, Qu L, Li HH. Fetal central nervous system anomalies: comparison of magnetic resonance imaging and ultrasonography for diagnosis. *Chin Med J (Engl)* 2006; **119:** 1272–1277.
21. Whitby EH, Paley MN, Sprigg A, Rutter S, Davies NP, Wilkinson ID, Griffiths PD. Comparison of ultrasound and magnetic resonance imaging in 100 singleton pregnancies with suspected brain abnormalities. *BJOG* 2004; **111:** 784–792.
22. Yin S, Na Q, Chen J, Li-Ling J, Liu C. Contribution of MRI to detect further anomalies in fetal ventriculomegaly. *Fetal Diagn Ther* 2010; **27:** 20–24.
23. Levine D, Barnes PD, Robertson RR, Wong G, Mehta TS. Fast MR imaging of fetal central nervous system abnormalities. *Radiology* 2003; **229:** 51–61.
24. Parilla BV, Endres LK, Dinsmoor MJ, Curran L. In utero progression of mild fetal ventriculomegaly. *Int J Gynaecol Obstet* 2006; **93:** 106–109.
25. International Society of Ultrasound in Obstetrics & Gynecology Education Committee. Sonographic examination of the fetal central nervous system: guidelines for performing the 'basic examination' and the 'fetal neurosonogram'. *Ultrasound Obstet Gynecol* 2007; **29:** 109–116.

SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Figure S1 Flow chart of studies included in the systematic review

Table S1 Characteristics of the included studies

Table S2 Studies excluded after detailed evaluation