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FULL PAPER

MRI of the foetal brain using a rapid 3D steady-state sequence

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Objective: To evaluate the capacity of a rapid T_2 weighted three-dimensional (3D) sequence to diagnose foetal brain abnormalities by comparing the results with current two-dimensional (2D) methods. We have also made assessments of the estimates of energy deposition using those methods.

Methods: 50 pregnant females were included in this study under the guidance of the institutional review board. All their foetuses had suspected brain abnormalities on antenatal ultrasonography or were at increased risk of a brain malformation based on the results of an earlier pregnancy. All the foetuses had a routine MR protocol that includes three orthogonal plane single-shot fast-spin echoes and 2D steady-state sequences. In addition, a 3D rapid steady-state sequence of the foetal brain was performed (acquisition time approximately 40s), and the standard and 3D sequences were reported independently and the results were compared. The specific absorption rate (SAR) predicted by the scanner was recorded in 12 cases in order to estimate the energy deposited by the three sequences.

Results: The 3D rapid steady-state sequences produced diagnostic-quality images in 41/50 (82%) cases. All the failures were in second trimester foetuses (9/26—35% failure rate). There was a discrepancy between the standard report and findings using the 3D sequence in 2/41 of the

foetuses with good-quality 3D imaging. The predicted SAR deposition of the 3D steady-state sequences was comparable with the single-shot fast-spin echo sequence.

Conclusion: Our initial assessments of a 3D rapid steady-state sequence to image the foetus are encouraging in terms of diagnostic information and acceptable energy deposition values. The high failure rate in second trimester foetuses probably relates to the greater mobility of the smaller foetuses, and improvements in the 3D sequence are required in terms of reduced acquisition time and higher resolution.

Advances in knowledge: We have shown that 3D T_2 weighted images of the foetal brain can be acquired in a clinical setting and produce diagnostic-quality imaging in a high proportion of cases. The success rate in acquiring diagnostic-quality images is related to gestational age. Good-quality images were obtained in all third trimester foetuses but only in approximately two-thirds of second trimester foetuses. This probably reflects the problem of the greater mobility of second trimester foetuses. 3D T_2 weighted acquisitions have great potential for improving the antenatal diagnosis of foetal brain abnormalities and may reduce the time that a pregnant female needs to spend on the MR scanner.

MRI of the foetus while *in utero* (iuMR) has become a valuable adjunct to antenatal ultrasonography over the past 10–15 years, particularly in cases of suspected brain pathology [1–6]. The most common approach to iuMR is to use sectional ultrafast imaging (broadly defined as the acquisition of one image per second) in order to reduce the effects of physiological movement of the anatomical target. This can be done using a range of MR sequences but the most commonly reported method is single-shot fast-spin echo (ssFSE). That sequence has the advantages of fast acquisition, one image acquired at a time and good T_2 weighted characteristics. T_2 weighted images are by far the

most valuable when imaging the foetal brain because it allows the highest tissue contrast in the low lipid and high water concentrations of the non-myelinated foetal brain.

Practically, iuMR is performed as an iterative method, in as much as the first sequence is run blindly (or at least using only the scout views for guidance) and then correcting the imaging planes based on the previous acquisition, assuming the foetal target has not moved. By this means, a series of two-dimensional (2D) image sets are acquired in the three orthogonal planes, although movement of the foetus can result in several attempts being required per plane.

Further refinements have seen the development of a range of sequences with different weightings [e.g. T_1 , fluid attenuated inversion recovery (FLAIR), T_2^* , diffusion weighted] that can be used in timescales appropriate for foetal studies. Another line of development is to look for alternative methods to obtain T_2 weighted images, one of the most promising of which is a rapid steady-state sequence, such as fast imaging employing steady-state acquisitions (FIESTA; GE Healthcare, Milwaukee, WI). FIESTA is a proprietary software name, referring to the use of 3D gradient echo steady-state free precession to acquire images of the foetal brain. This has been used primarily to produce good-quality 2D T_2 weighted images with reasonable tissue contrast in the foetal brain in times that are usually shorter than ssFSE sequences.

In this paper, however, we report our early experience of using FIESTA to obtain 3D MR data sets of the foetal brain. If this approach is successful, it would reduce the overall scan time for iuMR significantly and possibly reduce radiofrequency (RF) energy deposition in the foetus.

MATERIALS AND METHODS

Participants

The 3D FIESTA sequence described below was first used in our institution in August 2011, and we report the results of the first 50 cases used to study the foetal brain. Pregnant females with known or suspected brain abnormalities of the foetus as assessed by a foetomaternal expert on antenatal ultrasound were referred from several foetomaternal centres in the UK. Most of the females involved in this study were recruited as research cases under the guidance of the regional research ethics committee and provided written consent after full explanation, in line with the requirements at the time of recruitment. Those females were not paid for their involvement in the study but travel expenses were offered for themselves and a companion. The minority of examinations were performed as a clinical study and relevant review and approval was sought, and obtained, from the Institutional Clinical Effectiveness Unit and Research Department at the University of Sheffield, Sheffield, UK, in order to include those cases in this report.

MR methods

All iuMR examinations were performed within 5 working days of the referral from ultrasonography and were acquired on the same 1.5 T scanner (HDx; General Electric Healthcare, Milwaukee, WI) using either a flexible phased array body or a cardiac coil. The 3D FIESTA studies were performed at the end of the iuMR examination, after the routine sequences had been acquired (which always included 5-mm-thick ssFSE and 4.4-mm-thick 2D FIESTA in the three orthogonal planes—sequence summaries are presented in Table 1). They were run only once with no repeats. Diagnostic ssFSE sequences were obtained in all cases. For the ssFSE sequences, the refocusing angle was 90° , and the echo train length was variable: approximately 130. Field of view (FOV) was 360×360 mm, matrix size was 256×256 (giving an inplane resolution of 1.4 mm), and slice thickness was 3 mm and 5 mm. No parallel imaging was performed, and the number of excitations was 0.53.

For the FIESTA acquisitions, the refocusing angle was 60° . Other parameters included an FOV of 400×400 mm, a matrix size of 256×256 (giving an inplane resolution of 1.6 mm) and an interpolated slice thickness of 2.5 mm. There was no parallel imaging or partial filling of k -space.

The 3D FIESTA sequence was most frequently run in the plane axial to the foetal brain.

Other sequences such as ultrafast T_1 weighted, FLAIR and diffusion-weighted imaging were performed at the discretion of the radiologist supervising the study but are not included in further analysis in this paper. Total table occupancy time was approximately 30 min. The RF energy deposition for ssFSE, 2D FIESTA and 3D FIESTA sequences were studied in a random subgroup of 12 females using the estimates predicted by the proprietary software at the set-up stage of scanning.

Clinical reports were prepared in all cases by radiologists with experience in foetal MRI based on the standard iuMR protocols immediately after the examination. At the end of the study, a consensus was formed as to whether the 3D FIESTA images were of diagnostic quality or not (Table 2). This was done by an

Table 1. Summary of MR sequence data for single-shot FSE, 2D FIESTA and 3D FIESTA acquisitions used in this study, including estimates of specific absorption rate deposition

Parameter	Single-shot FSE	2D FIESTA	3D FIESTA
TR (s)	1782	Min (4.5)	Min (5.1)
TE (s)	914	Min (1.9)	Min (2.5)
Flip angle	—	60°	60°
Number of excitations	0.54	1.00	1.00
Slice thickness/gap (mm)	5.0/0.0	4.4/0.0	2.5/0.0
Approximate acquisition time (s)	29	18	40
Estimated mean RF energy deposition (W kg^{-1} in $n=12$)	1.95 ± 0.19	1.69 ± 0.17	1.85 ± 0.19
Estimated peak RF energy deposition (W kg^{-1} in $n=12$)	3.89 ± 0.35	3.47 ± 0.33	3.71 ± 0.38

2D, two-dimensional; 3D, three-dimensional; FIESTA, fast imaging employing steady-state acquisitions; FSE, fast spin echo; Min, minimum; RF, radiofrequency; TE, time of echo; TR, time of repetition.

Table 2. A summary of the diagnosis made on the routine iuMR and gestational age at the time of the examinations. The diagnostic information obtained from the 3D FIESTA studies are compared with the routine iuMR in the last column

Case	Gestational age (weeks)	Diagnosis on based on routine iuMR	Diagnosis on 3D FIESTA compared with ssFSE
1	33	Intracranial haemorrhage	Comparable abnormal
2	21	Microcephaly, intraventricular haemorrhage	Comparable abnormal
3	20	Microcephaly, hypoplasia of corpus callosum	Comparable abnormal
4	21	Moderate ventriculomegaly	Comparable abnormal
5	22	Agenesis of corpus callosum	Non-diagnostic 3D FIESTA
6	22	Agenesis of corpus callosum	Comparable abnormal
7	21	Semi-lobar holoprosencephaly	Comparable abnormal
8	27	Mild ventriculomegaly	Comparable abnormal
9	21	Cerebellar hypoplasia	Non-diagnostic 3D FIESTA
10	31	Chiari 2, myelomeningocele	Comparable abnormal
11	21	Hypoplasia of corpus callosum, Dandy–Walker spectrum	Non-diagnostic 3D FIESTA
12	27	Normal (scanned for possible vermian hypoplasia on ultrasound)	Comparable normal
13	28	Mild ventriculomegaly, germinolytic cysts	Comparable abnormal
14	22	Moderate ventriculomegaly	Non-diagnostic 3D FIESTA
15	32	Severe ventriculomegaly	Comparable abnormal
16	22	Agenesis of corpus callosum, heterotopia, Dandy–Walker spectrum	Heterotopia not shown on 3D FIESTA
17	21	Normal (family history of lissencephaly)	Comparable normal
18	29	Normal (scanned for possible cerebellar hypoplasia on ultrasound)	Comparable normal
19	21	Agenesis of corpus callosum	Comparable abnormal
20	28	Mild ventriculomegaly	Comparable abnormal
21	22	Cerebellar hypoplasia	Comparable abnormal
22	32	Unilateral polymicrogyria	Comparable abnormal
23	31	Mild ventriculomegaly, hydrops fetalis	Comparable abnormal
24	24	Normal (investigated for possible cerebellar hypoplasia on ultrasound)	Non-diagnostic 3D FIESTA
25	21	Mild ventriculomegaly, germinolytic cysts	Non-diagnostic 3D FIESTA
26	30	Mild ventriculomegaly	Comparable abnormal
27	32	Cerebellar hypoplasia	Comparable abnormal
28	34	Agenesis of corpus callosum	Comparable abnormal
29	22	Normal (investigated for possible cerebellar hypoplasia on ultrasound)	Comparable normal
30	31	Mild ventriculomegaly	Comparable abnormal
31	22	Moderate ventriculomegaly	Non-diagnostic 3D FIESTA
32	26	Mild ventriculomegaly	Comparable abnormal
33	28	Normal (family history of lissencephaly)	Comparable normal
34	24	Moderate ventriculomegaly	Comparable abnormal
35	21	Mild ventriculomegaly	Comparable abnormal
36	27	Closed-lip schizencephaly, heterotopia	Heterotopia not shown on 3D-FIESTA
37	30	Chiari 2, myelomeningocele	Comparable abnormal
38	21	Agenesis of corpus callosum	Non-diagnostic 3D FIESTA
39	20	Mild ventriculomegaly	Comparable abnormal

(Continued)

Table 2. (Continued)

Case	Gestational age (weeks)	Diagnosis on based on routine iuMR	Diagnosis on 3D FIESTA compared with ssFSE
40	29	Normal (investigated for possible cerebellar hypoplasia on ultrasound)	Comparable normal
41	20	Mild ventriculomegaly	Comparable abnormal
42	24	Normal (investigated for possible cerebellar hypoplasia on ultrasound)	Comparable normal
43	21	Cerebellar hypoplasia	Non-diagnostic 3D FIESTA
44	26	Mild ventriculomegaly	Comparable abnormal
45	22	Normal (family history of hemimegalencephaly)	Comparable normal
46	25	Agenesis of corpus callosum	Comparable abnormal
47	32	Unilateral polymicrogyria	Comparable abnormal
48	31	Mild ventriculomegaly	Comparable abnormal
49	35	Agenesis of corpus callosum	Comparable abnormal
50	31	Normal (investigated for possible cerebellar hypoplasia on ultrasound)	Comparable normal

3D, three-dimensional; iuMR, *in utero* MR; FIESTA, fast imaging employing steady-state acquisitions; ssFSE, single shot fast spin echo.

experienced paediatric/foetal neuroradiologist (PDG) and an MR radiographer experienced in foetal MR (DJ). All the 3D FIESTA examinations that were of diagnostic quality were reported by the radiologist (PDG) working using proprietary software (Advantage Windows; GE Healthcare, Milwaukee, WI). The software was used to reconstruct images in the three natural orthogonal planes with an isotropic resolution of approximately 0.8 mm. The relevant diagnostic features were recorded, and at a later date, the ssFSE and 2D FIESTA images were rereviewed by PDG without referring to the results of the 3D FIESTA studies. The comparison between the two sequences is recorded in Table 2 as “comparable normal”, “comparable abnormal” or with a description of any differences in the reports. No attempt was made to compare the ultrasound and iuMR findings; rather, the purpose of the study was to evaluate the diagnostic information of the 3D acquisitions with the current standard iuMR sequences.

RESULTS

26/50 examinations were performed on foetuses at 19- to 25-week gestational age and 24/50 at 26-week or more. The diagnoses made on the review of the ssFSE and 2D FIESTA sequences in the 50 foetuses are shown in Table 2. 10 foetal brains were considered to be normal, 18 showed isolated ventriculomegaly, 9 had agenesis/hypogenesis of the corpus callosum, 8 had cerebellar abnormalities, 3 had cortical formation abnormalities and 2 had intracranial haemorrhage. In all, 41/50 3D FIESTA studies were judged to be of diagnostic quality (82%) and all the non-diagnostic cases were in the 19- to 25-week gestational age group (failure rate 9/26—35%). All the 3D FIESTA sequences performed in the 26-week or more group were of diagnostic quality. There was a statistically significant difference between the chance of a 26-week or more foetus having an iuMR examination of diagnostic quality when compared with the 19- to 25-week foetuses (see Table 3, $0.01 > p > 0.001$, χ^2 1 df).

When 3D FIESTA examinations of diagnostic quality were obtained (41/50), comparable results with the routine iuMR sequences were reported in 39/41 cases (8 normal and 31

abnormal). Representative examples are shown in Figures 1 and 2. In the two cases in which the findings were discrepant, heterotopia was not recognised on the 3D FIESTA images. In all the cases with diagnostic-quality 3D FIESTA examinations, it was possible to use the proprietary software to segment out representations of the ventricular system as shown in Figures 2 and 3.

The estimated mean and peak specific absorption rate (SAR) levels for 12 females are presented in Table 1. The SAR levels for the 3D FIESTA acquisitions are comparable to those of the ssFSE sequences. The 2D FIESTA SAR levels are approximately 15% lower than the equivalent ssFSE sequences.

DISCUSSION

Current publications suggest that including iuMR in the diagnostic work-up of foetuses with known or suspected brain pathology is worthwhile in terms of improvements in diagnostic accuracy and subsequent effects on clinical management [1–6]. ssFSE is an ultrafast MR sequence that is the most frequently used for iuMR of the foetal brain according to the peer-reviewed literature. The resulting images are heavily T_2 weighted which, unlike when imaging the myelin-mature brain, provides optimal tissue contrast between the cerebrospinal fluid (CSF) and the future white matter and grey matter regions. This is because of

Table 3. The frequency of non-diagnostic 3D FIESTA studies in relation to gestational age of the foetus (see Results section for the description)

Study quality	iuMR cases performed at 19–24 weeks	iuMR cases performed at 25 weeks or over
Non-diagnostic 3D FIESTA	9	0
Diagnostic 3D FIESTA	17	24

3D, three-dimensional; FIESTA, fast imaging employing steady-state acquisitions; iuMR, *in utero* MR.

Figure 1. Case 30. A comparison between single-shot FSE images—(a) axial, (b) coronal, (c) sagittal—and equivalent sections reconstructed from a 3D FIESTA data set—(d) axial, (e) coronal, (f) sagittal—from a foetus diagnosed with isolated ventriculomegaly at 31 weeks' gestational age. The information obtained from the two methods was thought to be comparable. 3D, three dimensional; FIESTA, fast imaging employing steady-state acquisitions; FSE, fast spin echo.

the high proportion of water and absence of myelin. Full coverage of the foetal brain in each of the orthogonal planes using 5-mm-thick sections can usually be achieved in 20–30 s in foetuses of any gestational age. The short scan times are achieved because all the k -space data for one image is acquired in one time of repetition (TR) interval by using long echo trains (e.g. 130). As this technique acquires one image at a time, movement during an acquisition does result in all images being degraded, which helps to reduce artefact arising from foetal and maternal motion.

Refinements in iuMR techniques have subsequently concentrated on either extending the range of weightings of MR sequences that can be used in the “ultrafast” timescale or exploration of other ways of acquiring T_2 weighted images. There have been successes on both fronts; most departments offering iuMR imaging can now produce foetal images with T_1 , FLAIR, gradient echo T_2^* and diffusion weightings in reasonably short scan times. It is important to consider why alternative approaches to acquiring T_2 weighted images of the foetal brain may be useful. In general, the

Figure 2. Case 47. A foetus at 32 weeks' gestational age with extensive polymicrogyria of the right cerebral hemisphere showing comparable findings on single-shot FSE images—(a) axial, (b) coronal—and reconstructions from the 3D FIESTA data set—(c) axial, (d) coronal. (e) Frontal and (f) inferior projections of the ventricular system segmented from the 3D FIESTA using proprietary software. 3D, three dimensional; FIESTA, fast imaging employing steady-state acquisitions; FSE, fast spin echo.

quality of images of the foetal brain produced by ssFSE methods is good but the use of high echo train length sequences has some drawbacks in terms of T_2 contrast and energy deposition. The high number of echoes used in ssFSE sequences results in an image that is a composite of multiple echo times, which leads to “spectral blurring”, resulting in poor delineation of small structures with T_2 relaxation times that are similar. This is particularly relevant in second-trimester foetuses where definition of the transient structures of the developing cerebral hemispheres is important. One approach to rectify this in a foetus that is comparatively still is to use longer FSE acquisitions with short echo train lengths, although this is not applicable in the majority of cases.

Those issues motivated us to explore the utility of a family of gradient echo sequences using steady-state free precession principles. This approach has been used to produce 2D acquisitions of foetal anatomy [7] and real-time cine of foetal movement [8,9] but not for 3D acquisitions as far as we are aware. We used 2D FIESTA, which is a fully balanced steady-state coherent gradient echo sequence that produces images with a high signal-to-noise ratio (SNR) in ultrafast timescales. After empirical experimentation, we utilised a 2D FIESTA sequence with a flip angle of 60° , which has good contrast resolution and acquisition times that are usually 40% shorter than ssFSE sequences of equivalent anatomical coverage. One major advantage of FIESTA is a short TR, which allows good spin phase coherence, so preserving transverse

Figure 3. Case 36. A foetus at 27 weeks' gestational age with closed-lip schizencephaly in the left occipital lobe and periventricular heterotopia of the trigone and occipital horn of the left lateral ventricle. The heterotopia and the schizencephalic cleft are visible on single-shot FSE images (a-c), but the reconstructions of the 3D FIESTA data show the schizencephaly but not the heterotopia convincingly (d,e). (f) A superior projection of the ventricular system segmented from the 3D FIESTA that shows both the CSF in the cleft and the indentations on the ventricular system caused by the heterotopia. 3D, three dimensional; CSF, cerebrospinal fluid; FIESTA, fast imaging employing steady-state acquisitions; FSE, fast spin echo.

magnetisation to eliminate susceptibility artefacts. The T_1/T_2 ratios, rather than the T_1/T_2 differences, produce the resulting signal intensity, which is independent of TR. The SAR estimates produced by the scanner software are shown that energy deposition is approximately 15% lower for 2D FIESTA than equivalent ssFSE

sequences, and FIESTA 3D has similar energy deposition rates to ssFSE, as shown in Table 1. The ssFSE sequence used has a relatively long TR (1782 ms), in which the 180° refocusing pulses were applied approximately every 13 ms. FIESTA 3D had a much shorter TR and transmitted a 60° pulse every 5.1 ms. The shorter TR of the

FIESTA 3D sequence compensated for the lower flip angle used than that of the ssFSE sequence and resulted in the SAR deposition being roughly the same for the two sequence types.

One problem persists that is common for all sectionally acquired MR sequences used in foetal imaging, such as ssFSE and 2D FIESTA; namely, “wasted” images. The approach to imaging the foetal brain using those techniques is iterative in as much as the images acquired previously are used to define the next imaging plane and no foetal movement is assumed. This is often not correct, which results in the production of sequences that are not in the natural orthogonal planes and not useful diagnostically so the table occupancy for the pregnant female is increased. Sophisticated strategies have been developed to use those wasted images to reconstruct a 3D data set in order to post-process high-quality images in the orthogonal planes [10,11]. In this paper, however, we have applied a FIESTA sequence that allows true 3D acquisitions of the foetal brain in scan times of approximately 40 s. We used a partition thickness of 2.5 mm to reduce partial volume effects while maintaining the good high SNR. That data are imported into the proprietary software that allows reconstruction in any plane within a matter of seconds. It is also simple to segment projections of the cerebral ventricles with the same software in a similar timescale (Figures 2 and 3). It is also possible to export the data in order to use packages that segment the brain away from the skull and external CSF in order to produce surface images of the brain.

The technique is not mature and there are still major drawbacks at this stage. The relatively long acquisition times (40 s) mean that an unacceptably high proportion of examinations did not produce images of diagnostic quality because of degradation owing to foetal movement. This occurred in 18% of all cases and in 35% of second-trimester cases. All 3D FIESTA acquisitions

obtained in third-trimester fetuses produced images of diagnostic quality. We suspect that this reflects the reduced degree of foetal movement because of the comparatively restricted space *in utero* in the third trimester. Future developments will require a reduction in scan times to 15–20 s. The second difficulty concerns image resolution. There is no doubt that the contrast resolution is not as good on 3D FIESTA than on ssFSE or even the 2D FIESTA sequences, and the anatomical resolution is also in need of improvement. The 3D FIESTA sequence used in this study did not produce anisotropic data sets because the out-of-plane resolution came from 2.5-mm partition thicknesses as opposed to the inplane resolution of approximately 1.0 mm. As a result, a reconstructed image that is closer to the plane of acquisition of the original data has high “diagnostic quality” compared with those further from that plane, as is demonstrated in Figures 1–3.

From the point of view of clinical utility, however, when 3D sequences of acceptable quality were obtained, the majority of the pathology described on ssFSE sequences was independently demonstrable on 3D FIESTA reconstructions. The only pathologies that were not described on FIESTA were subependymal heterotopia in two fetuses (Cases 16 and 36), which were both subtle abnormalities on ssFSE and 2D FIESTA. Case 36 illustrates an important point about slice thickness.

In conclusion, we have shown that it is possible to produce acceptable T_2 weighted images of the foetal brain from 3D FIESTA sequences in a high percentage of cases, and a significant proportion of pathology was shown as well as on routine sequences. Improvements in acquisition times and anatomical resolution are needed before 3D FIESTA can be seen as a frontline imaging tool for the foetal brain.

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