T2-Weighted Fast MR Imaging with True FISP Versus HASTE: Comparative Efficacy in the Evaluation of Normal Fetal Brain Maturation

**OBJECTIVE.** This study compares the relative efficacy of two fast T2-weighted MR imaging techniques—fast imaging with steady-state free precession (true FISP) and half-Fourier acquisition single-shot turbo spin-echo (HASTE)—in the evaluation of the normal fetal brain maturation during the second and third trimesters of gestation.

**SUBJECTS AND METHODS.** The brain maturation of 10 normal nonsedated fetuses (5 during the second trimester and 6 during the third trimester of gestation [1 fetus underwent 2 examinations]) was examined by both techniques using a Vision+ 1.5-T MR system. We specifically looked for developing events, including white matter myelination, neuronal migration, and cortical sulcation. Image quality was graded according to the presence or absence of undesirable blurring.

**RESULTS.** The specific absorption rate was lower for true FISP than for HASTE by a factor of 3 at equivalent imaging conditions. HASTE and true FISP provide comparable image quality in the second trimester when myelination of the cerebrum has not begun. Neuronal migration could be recognized as hypodense bands on both sequences during the second trimester. Myelination beginning at the third trimester was better delineated with true FISP than with HASTE because of point spread function–related blurring effects inherent in HASTE that hampered visualization of short-T2 structures. Cortical sulcation was well delineated by both sequences.

**CONCLUSION.** With relatively superior image quality and significantly lower radiofrequency absorption than HASTE, true FISP is a safer and more effective alternative in the prenatal evaluation of normal fetal brain.

R imaging is now considered an important adjunct to sonography in the evaluation of abnormalities of the fetal central nervous system (CNS) [1, 2]. Recent reports document the importance of fetal MR imaging, which could directly affect fetal management or surgical decision [3, 4]. As a consequence, technical improvements of fetal MR imaging may have a strong impact on fetal care. Involuntary motion, however, has been a major problem necessitating the sedation of mother or fetus to obtain high-quality MR images [5, 6], with additional undesirable risks. Therefore, fast imaging sequences that allow effective “freezing” of motion, while providing images of diagnostic quality, are of great interest.

The spin echo–based half-Fourier acquisition single-shot turbo spin-echo (HASTE) technique has recently been reported to overcome such a problem [7, 8]. The fetal CNS anatomy could be clearly depicted in fetuses during the third trimester [2, 9], and the diagnosis with prenatal MR imaging was reportedly improved [2, 10]. The capability of generating T2-weighted images that clearly delineate fetal anatomy [7] makes HASTE ideally suited for such an application. However, being a single-shot technique with only one radiofrequency excitation pulse generating a long train of spin echoes, HASTE may have potential problems in degradation of spatial resolution caused by T2-related point-spread-function blurring [11], causing possible loss of small tissues having a short T2 [12]. As a consequence, there remains room for further improvement of fetal MR imaging.

The fast imaging with steady-state free precession technique (true FISP) [13] based on gradient echo is another fast sequence that could achieve a scanning time of 1 sec per slice with a high signal-to-noise ratio. Originally designed for improved visualization of the cerebrospinal...
fluid [13], true FISP has rarely been used in clinical practice because of its sensitivity to field heterogeneity that leads to banding across the image field of view [14]. With new advances in gradient coil and shimming technology, the banding artifacts caused by field heterogeneity have become less severe with a reduction in the TR [15]. Recent work suggests that true FISP may now prove useful in clinical practice [16–18], including fetal imaging. Because of the multishot nature of true FISP that affords equal K-space weighting and hence absence of point-spread-function blurring, we hypothesize that true FISP has unique advantages over HASTE in fast fetal imaging. The objective of this study is to compare true FISP with HASTE in the evaluation of fetal brain maturation during the second and third trimesters of gestation. A theoretic discussion of true FISP contrast in the developing brain is also provided.

Subjects and Methods

Ten fetuses (all singlets) of 20–35 weeks of gestation were included in this study. One fetus underwent consecutive examinations during the second and third trimesters, making the number of examinations 11 (five during the second trimester and six during the third trimester). The gestational ages were based on the last menstrual periods and were also calculated at sonographic examinations performed in the same week as the MR imaging studies. All fetuses referred for possible CNS abnormalities had inconclusive sonographic results (four had suspicious ventriculomegaly and the other six had poorly delineated brain structures, including the corpus callosum and gyral anatomy). Fetuses were judged as normal by MR imaging interpretation and postnatal sonography. All fetuses underwent imaging examination using both sequences in the same examination. The mothers were in a supine or oblique position. Informed consent was obtained from all mothers who entered the study. The local institutional review board approved the imaging protocol.

The CNS of the 10 healthy fetuses was examined using both T2-weighted HASTE (240 × 256 matrix, 1-sec scan per slice including a 400-msec scan delay) and true FISP (240 × 256 matrix, 1-sec scan per slice including 200-msec scan delay) on a Vision+ 1.5-T MR imaging system (Siemens, Erlangen, Germany) providing a maximum gradient strength of 25 mT/m. The body coil was used for excitation, and a four-element pelvic phase array coil was used for signal receiving. Slice thickness was 5–6 mm, with 11–13 sequentially acquired imaging slices to cover the entire fetal brain, resulting in about 13 sec of scanning time for each sequence. The field of view was 38 cm with a 240 × 256 image matrix, yielding about 1.5-mm in-plane resolution. For HASTE imaging, an effective TE of 64 msec, known to provide T2-weighted contrast suitable for fetal imaging [7, 19, 20], was used. The flip angle of the refocusing pulses was reduced from 180° to 130° to lower specific radiofrequency absorption with only a slight sacrifice of signal-to-noise ratio [7]. For the true FISP sequence, a TR of 4.8 msec and a TE of 2.3 msec were used. The flip angle of the excitation pulses was chosen to be 70° with 180° phase alternation [15]. Readout bandwidth was 650 Hz/pixel in both techniques, leading to 10.3 mT/m gradient strength for the chosen field of view. Automatic shimming was performed in all cases. No breath-holding by the mother was used. The specific radiofrequency absorption rate was computed using the manufacturer-provided tools for both sequences. Fetal brain images were acquired using both techniques in three planes orthogonal to the fetal brain. The entire examination time, including shimming, the localizing scan, and patient preparation, was about 20 min.

MR images were separately filed for true FISP and HASTE sequences for each fetus. The imaging parameters were removed from the hard-copy films. Two reviewers unaware of results of MR imaging sequences independently identified the following developing brain structures according to the previous gestational guidelines for fetal CNS:

- White matter myelination.—The time table of white matter myelination in the cerebrum and brain stem was based on the studies by Hasegawa et al. [21] and Friede [22]. Myelination can be seen in the cerebellar connections and the tegmentum of pons at 22–24 weeks of gestational age [22]. Beginning at 25 weeks, myelination occurs in the globus pallidus, the posterior internal capsule, and the thalamus [21].

- Basal ganglia and thalami.—The gestational age and MR imaging appearance of basal ganglia and thalami were compared with those in the in vitro MR study by Brisse et al. [23]. From 16 to 22 weeks, the signal intensity of the pallidum and the thalamus is isointense with that of white matter. The signal becomes low on T2-weighted images from 27 to 34 weeks.

- Germinal matrix.—According to Brisse et al. [23], germinal matrix can be seen as a low signal on T2-weighted images at the inner layer of the cerebral mantle from 16 weeks’ to 27 weeks’ gestation.

- Neuronal migration.—Neuronal migration is determined by the multilayered appearance of the cerebral mantle on T2-weighted images. Depending on the gestational age, three layers (inner germinal matrix, intermediate migrating wave of neurons, and outer immature cortex) were observed at 16 weeks, four layers at 19–22 weeks, and two layers (inner white matter and outer cortex) at 34 weeks [23].

- Cortical sulcation.—The gestational milestones of cortical sulcation were compared with gestational ages determined in anatomic specimens by Chi et al. [24] and in the MR imaging study by Levine and Barnes [25]. The sylvian fissures can be seen on fetal MR images as early as 16–17 weeks of gestation. At 18–19 weeks, sulci such as calcarine, parietooccipital, and circular sulci are visible.

The presence or absence of the undesirable blurring effect was recorded for each set of images obtained with the two sequences. Image quality was graded for a particular brain structure or the presence of the blurring effect as “−,” “R,” and “W” for “not recognized,” “recognized,” and “well recognized,” respectively. Disagreement of opinion on the presence or absence of a particular developing brain structure, or of blurring effect with each sequence, was then discussed, and a consensus was reached.

TI and T2 relaxation times in the fetal brain were estimated using double-contrast turbo spin-echo sequences (effective TE, 85 and 170 msec) with a different TR (1000, 2000, and 3000 msec) for a calculation of true FISP contrast in the fetal brain. Note that because the turbo spin-echo sequences are multishot in general, the scanning time of 20 sec or longer resulted in image-quality deterioration because of fetal motion. Furthermore, the position of the fetus may change between scans. Therefore, the TI and T2 values reported in this study are rough estimates only and may be subject to inherent inaccuracies.

Results

All fast imaging examinations of the fetal CNS using HASTE and true FISP were successful. However, the measurements of TI and T2 were hampered by motion artifacts. In images that were free of substantial motion artifacts, the TI and T2 were estimated to be about 2500 ± 600 and 400 ± 150 msec (mean ± fitting uncertainty), respectively. Computation of radiofrequency absorption showed true FISP to be lower in specific absorption rate than HASTE by a factor of about 3 (average partial-body specific absorption rate: 0.69 versus 1.93 W/kg, and average local specific absorption rate: 1.73 versus 4.81 W/kg for true FISP and HASTE, respectively).

The results of comparison between true FISP and HASTE for assessing brain maturation of each individual fetus are listed in Table 1. For the second trimester group (Figs. 1 and 2), the only recognizable myelination was in the tegmentum of the pons (Fig. 1), which was better delineated with true FISP than with HASTE. Both sequences revealed poorly demarcated basal ganglia and thalami at the second trimester because of their signal intensities being isointense to the internal capsules and adjacent rows of migratory neurons. The concentric waves of migrating neurons, which with the germinal matrix and cortical plate compose four typical layers of cerebral mantle that had been shown in vitro with histologic proof [23], were equally well recognized on both sequences during the second trimester (Fig. 2). The cortical sulcation was equally delineated by both true FISP and HASTE. Blurring effects were mostly absent in images acquired by both sequences except in the myelinated tegmentum of the pons, where only the HASTE images showed minor blurring. However, the parietooccipital
and calcarine sulci that were reported to be visible on MR imaging at 22 weeks of gestational age [25] were not recognized with either true FISP or HASTE.

In contrast to the immature brain, white matter myelination was noted in the basal ganglia, optic radiation, perirolandic gyri (Fig. 3), hippocampi, and brainstem at the third trimester of gestation. True FISP consistently showed better the myelination and definition of the deep-seated nuclei than did the HASTE sequence during the third trimester. The concentric waves of migrating neurons were not recognized during the third trimester with either technique. The cortical sulcation was well delineated by both true FISP and HASTE. Significant blurring of the myelinated white matter was found along the phase-encoding direction in the HASTE images (Fig. 3a) but not in the true FISP images (Fig. 3b).

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<tr>
<th>Fetus</th>
<th>Gestational Age</th>
<th>Sequence</th>
<th>White Matter Myelination</th>
<th>Basal Ganglia and Thalami</th>
<th>Germinal Matrix</th>
<th>Neuronal Migration</th>
<th>Cortical Sulcation</th>
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Note.—FISP = fast imaging with steady-state free precession, HASTE = half-Fourier acquisition single-shot turbo spin echo, dash (—) = not recognized, W = well recognized, R = recognized.

aFor brainstem myelination only.
bFor both brainstem and cerebrum myelination.
Discussion

Two fast imaging sequences for examining normal development of fetal CNS—true FISP and HASTE—were compared in this study. Both techniques offer scanning times of about 1 sec per slice. Images were free from motion-induced degradation, thereby obviating sedation. The fetal brain images acquired with true FISP showed superior conspicuity to the HASTE images during the third trimester when the specific radiofrequency absorption rate was shown to be substantially less than that of HASTE. This is consistent with the theoretical prediction that the specific radiofrequency absorption rate scales roughly to the square of the flip angle for the fixed pulse width. Because fetal imaging studies using HASTE sequences showed safe specific radiofrequency absorption rate well within the limits specified by the British National Radiological Protection Board [7, 8, 20], the specific radiofrequency absorption rate of true FISP is thought to be within safe limits.

The superior image quality of the fetal brain exhibited by true FISP relative to HASTE deserves some discussion. Myelination of the white matter causes shortening of both T1 and T2, possibly because of a reduction in the content of free water [26]. In our study, T1 and T2 of immature white matter were about 2500 and 400 msec, respectively, whereas in the adult white matter T1 and T2 have been reported to be 900 and 80 msec, respectively, at 1.5 T [13]. As a consequence, visualization of myelination during brain development (i.e., change of T2 from 400 to 80 msec) necessitates T2 weighting with a TE of 100–150 msec [27]. With a total scanning time of about 600 msec and a TE of 100–150 msec, a substantial portion of data acquired in HASTE for the outer portion of the K-space is from the late echoes. Therefore, the single-shot HASTE suffers from continuous T2 decay, causing inevitable point-spread-function blurring [11, 12], which is detrimental for delineating short-T2 tissues such as the myelinated white matter. This blurring is especially evident in our study in which an effective TE of 64 msec was used (Figs. 1A and 3A). On the other hand, true FISP uses steady-state acquisition that affords equal K-space weighting. Hence, no T2-related point-spread-function blurring is expected. Our imaging results indicate that true FISP is superior to HASTE in evaluating fetal CNS during the third trimester, consistent with the previously noted theoretic prediction.

During the second trimester of gestation for the immature brain, in which myelination has not begun [21], T2 is 400 msec. Compared with imaging of fetal brain during the third trimester, point-spread-function blurring in HASTE occurs

Fig. 2.—Neuronal migration in normal fetus at 22 weeks’ gestation. 
A, Magnified coronal half-Fourier acquisition single-shot turbo spin-echo MR image shows four-layer pattern of cerebral mantle comprising, from inner to outer layers, germinal matrix, row of migrating neurons, intermediate zone, and immature cortex. Arrows indicate boundaries between layers. 
B, Magnified coronal fast MR image with steady-state free precession at same level as A shows comparable imaging quality in supratentorial anatomy depiction during second trimester. Arrows indicate boundaries between layers.

Fig. 3.—Perirolandic myelination in normal fetus at 33 weeks’ gestation. 
A, Magnified axial half-Fourier acquisition single-shot turbo spin-echo MR image suffers from severe blurring along phase-encoding direction (arrows). Myelination was distorted by blurring and hence was less conspicuous. 
B, Magnified axial fast MR image with steady-state free precession at same level as A clearly shows early perirolandic myelination as hypointense signal (arrowheads). Note that fat-water boundary was conspicuously delineated in this image because of out-phase nature of TE (2.3 msec) in gradient-echo images.
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found to be insignificant, if not entirely absent, to a negligible extent. The difference between the two techniques compared in this study is thus theoretically expected to be less significant. Our study images acquired using HASTE and true FISP during the second trimester were found to be almost visually comparable in the cerebrum, again consistent with the explanation of T2-related point-spread-function blurring. However, the delineation of early myelination in the tegmentum of the brainstem by HASTE is still degraded by the undesirable blurring effect in our patients (Fig. 1A). Evaluation of cortical maturation was equally effective with both sequences at different gestational ages. The reason both sequences failed to show the parietooccipital and calcarine sulci in fetuses at 20–22 weeks of gestational age can be explained by the slice thickness (5-6 mm) we used, compared with the 3-5 mm described previously [25]. The multisot nature of true FISP, which affords equal K-space weighting, produced slightly better delineation of the multilayer cellular migrational process than HASTE (Fig. 2). Hence, we consider true FISP to be a better alternative in the examination of normal fetal brain development.

However, the contrast in true FISP is known to be T1/T2- rather than T2-weighted [13, 15]. Such a property yields poor contrast between gray and white matter in the adult brain, as already noted in previous studies [13]. To see whether this contrast mechanism provides differentiation of the myelination process for the developing brain, we plotted the theoretically derived signal change as a function of T1/T2 in Figure 4 for true FISP at three excitation flip angles, using the formula from the existing literature [13, 15]. The horizontal scale corresponds to the myelination process, which causes an increase of T1/T2 from 2500/400 msec (approximately 6.3%) to 900/80 msec (approximately 11.3%). Because “T1 is much greater than T2” is true for adult white matter, changes in T2 essentially dominate. Thus for the 70° flip angle used in this study, mature white matter has a signal intensity 50% less than that in nonmyelinated white matter (Fig. 4). This decreasing change in true FISP signal thus provides conspicuous contrast to delineate myelination as a low-signal-intensity area, similar to that on a T2-weighted image with a TE of 100 msec. Therefore, the intrinsic T1/T2 contrast independent of TR and TE [15, 28] also renders true FISP suitable for the evaluation of fetal CNS during early myelination.

The banding artifacts inherent in true FISP images at high field (e.g., 1.5 T) [13, 14] were found to be insignificant, if not entirely absent, in this study. Because image banding in true FISP is a result of nonuniform steady-state free precession within one TR [14, 15, 28], the absence of banding in our study is believed to arise from improvements in gradient coil design (which allows reduction of TR) and shimming technology (which increases field homogeneity). In particular, the choice of shimming methods (such as a local shim versus a three-dimensional shim) may play an important role in the success of true FISP scanning. The effect of the steady-state-free-precession angle on true FISP signal at a 70° flip angle was plotted with T1 and T2 values estimated in this study using the formula in the literature (Fig. 5) [13, 15]. In this figure, one notices that the signal is relatively uniform for all brain tissues, with about 90° of tolerance in the steady-state-free-precession angle [13] if 180° phase alternation is used for radiofrequency excitation [15]. In fetal brain imaging, the amniotic fluid surrounding the fetus, along with the spherically shaped abdomen of the mother, provides a homogeneous environment with minimal susceptibility effects from the air-tissue interface. Consequently, a line width (calculated at one tenth of maximum) of 1.0 ppm can be routinely achieved for the mother’s abdomen with automatic three-dimensional shimming, corresponding to about 64 Hz at 1.5 T. Banding-free images can thus be obtained at a TR of about 8.0 msec or less. The use of 4.8 msec TR in this study fulfilled such a requirement. Therefore, the true FISP images exhibited minor or even no banding artifacts in our study.

We conclude that true FISP is a promising tool for visualizing fetal brain development. True FISP offers unique features of rapid scanning, effective freezing of fetal motion, high signal-to-noise ratio at a short TR [13], high amniotic fluid signal outlining the fetus, and high T1/T2 contrast to visualize the myelination process. Compared with techniques based on single-shot turbo spin-echo such as HASTE, true FISP provides high-quality images at a significantly lower specific radiofrequency absorption rate with no
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References

22. Friede RL. Developmental neuropathology, 2nd ed. Berlin: Springer-Verlag, 1989;2–10