Short communication

Failure to detect intrauterine growth restriction following in utero exposure to MRI

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Abstract. Echo planar imaging is a form of MRI with short image acquisition times, which permits in utero fetal imaging without motion artefacts. Echo planar imaging has been used to measure accurately fetal organ volume and to assess placental function. Two small animal studies have suggested the possibility of intrauterine growth restriction consequent upon MRI. We thus performed a prospective study of pregnancies in which fetuses were exposed to echo planar imaging, compared with a control group in which there was no in utero echo planar imaging exposure. There were no significant differences between the groups when maternal age, parity, proportion of smokers and proportion of Caucasian women were compared. Although the gestational age of delivery was lower in the echo planar imaging group, the proportion of women delivering prematurely was not significantly different. Although infant birthweights were significantly lower in the MRI group, the corrected birthweight for gestational age centiles (individualized birthweight ratio) was not significantly different between the two groups. In utero exposure to echo planar imaging thus did not have a marked effect on intrauterine fetal growth. A 10 year follow-up study of all infants imaged in utero is being performed.

Conventional MRI does not provide clear fetal images due to long imaging times and fetal movement which result in blurred images. It is possible to produce high quality images of the fetus using a high speed imaging technique such as echo planar imaging (EPI), FLASH [1] or HASTE [2]. EPI is a form of MRI, developed in Nottingham, that gives short image acquisition times. EPI permits a fetus to be investigated rapidly whilst obtaining a sequence of images that are free from motion artefacts. Each image is displayed as it is acquired in real time. The development of EPI has led to a clear demonstration of fetal anatomy and accurate organ volume measurements of organs such as fetal liver and fetal lung [3]. The use of the technique to estimate fetal weight has opened up the possibility of more accurate estimations than are possible by ultrasound. EPI has also been used to assess placental function and uterine artery blood flow which has the potential to be used in the management of intrauterine growth restriction (IUGR) and pre-eclampsia [4].

EPI has the potential to aid the management of compromised pregnancies. However, prior to clinical application, the safety of the technique must be fully established. MRI does not involve exposure to ionizing radiation or radio-isotopes. EPI involves the application of three different magnetic fields: a strong (0.5 T) static magnetic field, a rapidly oscillating (0.5 kHz) magnetic field gradient, and radiofrequency magnetic fields. Under extreme conditions, all these fields could potentially cause harmful acute effects. In particular, the radiofrequency fields can cause tissue heating, and electric fields induced by the oscillating magnetic fields can cause neural stimulation. However, these effects do not occur under normal conditions of fetal scanning. Moreover, a combination of oscillating magnetic field gradients and a static magnetic field give rise to a loud acoustic noise.

Although many animal studies have shown no effects of in utero exposure to MRI, there have been two small studies which have suggested that in utero exposure may result in IUGR. Carnes et al studied the effects of exposure to high field MRI on fetal growth in the mouse [5]. A high strength magnet (4.7 T) was used and exposures were of eight hours duration. Fetal weights of the exposed mice were between 11% and 17% lower than those of control fetuses. Crown–rump lengths were...
similarly reduced in animals exposed at 9 days. No effect was found after exposure at day 9 and day 12 or day 12 alone. Tyndall demonstrated similar significant effects on fetal crown–rump lengths when pregnant mice were exposed to a 1.5 T magnet [6]. Tyndall did not report raw data, but did find that the proportion of fetuses with low crown–rump lengths was increased following in utero exposure to MRI [6]. No harmful effects to adults or infants have been associated with MRI and indeed a long-term biological effect of MRI would be very difficult to explain. However, there is a marked paucity of studies concerning safety of MRI in animal or human pregnancy. The only published study of the safety of MRI in human pregnancy was a 3 year follow-up uncontrolled observational study of 20 children who were imaged in utero. All 20 pregnancies had been deemed to be “abnormal” at the time of exposure to MRI, and no disease or disability that was attributable to MRI was identified [7].

We have thus compared the outcome of 74 pregnancies in which fetuses were exposed to EPI, with the outcome of a control group in which there was no in utero EPI exposure.

**Method**

74 pregnant women underwent exposure to EPI as part of a study to determine the potential clinical applications of EPI in pregnancy. All pregnancies were singleton and none were complicated by hypertension. These women were volunteers recruited in response to advertisements in the antenatal clinic at Nottingham City Hospital. Ethical permission for imaging such women was obtained from the local Hospital Committee. Informed written consent was obtained from all women. Volunteers underwent up to five serial scans: the first scan being at approximately 20 weeks’ gestation and the final scan being between 36–40 weeks’ gestation. Gestational age was determined by a second trimester ultrasound scan (± 7 days). All images were obtained with a 0.5 T super-conductive magnet using the modulus-blipped echo MRI spin system [3]. The radiofrequency, gradient and static magnetic field exposures were within the safety guidelines of the National Radiological Protection Board. A control group was selected from women who attended for a detailed second trimester ultrasound scan at the same time as women who subsequently underwent EPI scanning. In each group of 10 women having a detailed ultrasound scan, the two most closely matched women were chosen as controls. Matching was achieved using a scoring system based on maternal age, parity, ethnic origin, smoking history and post code.

Outcome measures for MRI and control pregnant women were gestational ages at delivery, APGAR scores at 1 and 5 min, admission to the Neonatal Unit, method of delivery, birthweight and individualized birthweight ratio (IBR). IBR is a ratio relative to predicted birthweight (calculated using gestational age to delivery, parity, ethnic origin, maternal height and booking weight and fetal sex). IBR enables a more accurate prediction of pregnancies which end in a poor outcome than birthweight for gestational age alone [8].

**Results**

The characteristics of the MRI group and the control group are detailed in Table 1. There were no significant differences between the groups when maternal ages and parities were compared (p > 0.05, Student’s t-test), or when the proportion of smokers and Caucasian women were compared (p > 0.05, Fisher’s exact probability test).

Infant birthweights were significantly lower in the MRI group compared with the control group (Table 1, p < 0.05). However, the gestational ages at delivery were also lower in the MRI group (p < 0.05) and no significant differences in the IBR were found between the two groups (p > 0.1). There was no significant difference in the proportion of women delivering prior to 37 weeks gestation when the two groups were compared (p > 0.1). No significant differences were found when the APGAR scores at 1 and 5 min, the admission rates to the Neonatal Unit and the proportions of women who underwent elective or emergency operative or normal deliveries were compared.

**Discussion**

IUGR (determined on the basis of IBR) was not found in a significantly greater proportion of

<table>
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<tr>
<th>Table 1. Characteristics of the MRI and control groups</th>
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<tr>
<td><strong>MRI group</strong></td>
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<tr>
<td>(n = 74)</td>
</tr>
<tr>
<td>Maternal age (years)</td>
</tr>
<tr>
<td>Nulliparous women</td>
</tr>
<tr>
<td>Smokers</td>
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<tr>
<td>Gestation at delivery (weeks)</td>
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<tr>
<td>Delivery &lt; 37 weeks</td>
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<tr>
<td>Infant birthweight (kg)</td>
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<td>IBR (centile)</td>
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<td>APGAR score at 1 min</td>
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<td>APGAR score at 5 min</td>
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<td>Admission to the neonatal unit</td>
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Values are means ± standard error of the mean.
pregnancies exposed to MRI compared with control pregnancies. This finding is in keeping with the known biological effects of MRI. In contrast, two small previous rodent studies have suggested an effect of magnetic resonance exposure on birthweight.

The significantly lower infant birthweights in the MRI group were due to significant lower gestations at delivery. Corrected birthweights did not differ between the two groups. MRI has not previously been reported as causing a diminution in gestational age, although this is one explanation for the diminished birthweight in the previously reported animals studies [5, 6]. An alternative explanation is that the difference in gestational age may represent greater medical input in the MRI group. The obstetricians dealing with the pregnancies were not blind to which patients were in the MRI group and which were control patients. The MRI group were reviewed by an obstetrician on each occasion when they attended for a scan, and the induction rate was significantly higher in the MRI group (17%) than in the control group (11%). The lower gestational age at delivery was not clinically important, and the proportion of women delivering prematurely prior to 37 weeks’ gestation did not differ significantly.

There was one neonatal death and one stillbirth in the pregnancies studied, both of which were in the MRI group. The first of these occurred at 35 weeks’ gestation, following a massive placental abruption in an otherwise uncomplicated pregnancy. The woman was known to have a subacute uterus; however, the IBR was below the tenth centile. This woman had last undergone EPI scanning more than 2 months prior to the abruption. The second case was an unexplained stillbirth at 38 weeks’ gestation. This woman had a previous poor obstetric history; however, the IBR was above the sixtieth centile. This woman had last undergone EPI scanning 5 weeks prior to the stillbirth.

It is clearly never possible to conclude from a single study such as this that EPI scanning in pregnancy is safe. Moreover, all the scans in this study were performed in the second half of the pregnancy. However, in utero exposure to EPI did not have a marked effect on intrauterine fetal growth. In view of the paucity of available data regarding the safety of MRI in pregnancy, allied to the increasing number of centres which are performing fetal imaging using this technique, it is ethically imperative that all groups analyse and report the effects of in utero imaging. A 10 year follow-up study of all infants imaged in utero is currently under way at our centre.

**Acknowledgments**

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**References**