Magnetic Resonance in MiGTOFU Trial

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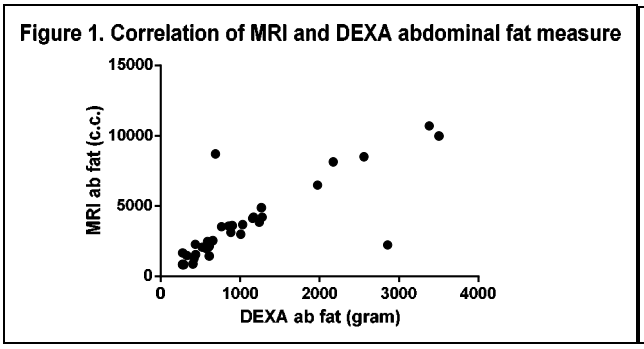
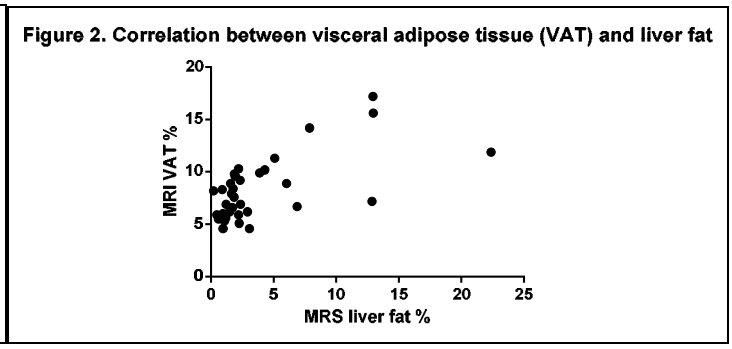
Target audience: Clinical and research endocrinologists, researchers in the area of obesity, diabetes and metabolism, magnetic resonance technologists

Purpose: The Metformin in Gestational diabetes (MiG) trial prospectively compared pregnancy outcomes in women with gestational diabetes (GDM) randomised to either metformin or insulin treatment (1). A follow-up – MiG The Offspring Follow Up (MiGTOFU) study at two years of age compared total and regional body composition by dual Xray absorptiometry (DEXA) between the two treatments and found no difference (2). The current follow-up study is to compare the adiposity, including intra-abdominal and liver fat, of the 7-9-year-old children of the MiG trial. Abdominal fat distribution was measured by magnetic resonance imaging (MRI), liver fat percentage by magnetic resonance spectroscopy (MRS) and total and abdominal body fat by DEXA. We have now measured one-third of the children (n=34), and hereby report the MR methods and preliminary results.

Methods: Children were positioned on the table in a supine position then moved into a 3 Tesla Siemens MRI system. A sagittal localizing image was acquired from 5.0 mm thick sections from diaphragm to pelvis. The field of view ranged from 30 to 50 cm, dependent on body thickness. Phase encoding was in the anteroposterior direction to minimize the effects of motion-induced phase artefacts and signal averaging (four) was applied to reduce the effect of motion-related artefacts. In addition, respiratory gating was used to combat motion induced artefacts and to reduce the blurring of fat boundaries in the anterior region of the abdomen. A 3D dual gradient-echo sequence acquired water/fat images in one acquisition using a 2-point Dixon technique. Images were acquired using a T1-weighted spin echo pulse sequence with a TR of 6.5 msec and a TE out of phase/in phase, 2.4/4.8 msec, flip angle 12 degrees, matrix 256 x 128, and 0.7 number of excitations. The actual scan time for abdominal fat assessment in each child was less than 30 seconds apart from scout imaging and section planning. Visceral fat and subcutaneous abdominal fat were distinguished through image processing, and the amounts/volumes of these compartments were calculated. After the abdominal scan, the child stayed in the scanner for a further 12 minutes and MR proton spectroscopy was performed to determine the liver fat content. A voxel of the size of 1.5 x 1.5 x 1.5 cm^3 was selected within the right lobe of the liver using images acquired from the abdominal scan. MRS of the selected voxel was performed. The spectrum was recorded using the stimulated-echo acquisition mode sequence, with an echo time of 20 msec, a TR of 3000 msec, a mixing time of 30 msec, 1024 data points over 1000 kHz spectral width with 32 averages. Water-suppressed spectrum with 128 averages was also recorded to detect weak lipid signals. Area under the curve (AUC) of water peak and fat peak was calculated from non-water-suppressed and water-suppressed spectra, respectively. Liver fat was presented as percentage volume/volume. The total time for the child and parent(s) to be in the examination room was around 30-35 minutes. All images were obtained under free-breathing conditions.

Results: Thirty four out of 36 children provided images and spectra of a quality acceptable for processing. For total abdominal fat amount, data acquired by MRI was tightly correlated to data acquired by DEXA, with $r^2 = 0.65$ (Figure 1). Intra-abdominal fat percentage acquired by MRI significantly correlated to liver fat acquired by MRS, with $r^2 = 0.39$ (Figure 2).





Discussion: Increased accumulation of intra-abdominal and liver fat has been recently emphasized as indicators of type 2 diabetes risk (3). Using MRI and MRS to successfully measure those parameters in children of MiGTOFU trial will provide valuable information about fat distribution in cohorts treated with different medication (metformin *vs*. insulin). The hypothesis is that the children of mother's with gestational diabetes who were treated during pregnancy with metformin will have a more favourable distribution of fat than those whose mothers were treated with insulin.

Conclusion: In free-breathing children valid MR measures of abdominal and liver fat have been developed.

Reference: 1) Rowan et al., 2008, *N Engl J Med* **358**: 2003-15. 2) Rowan et al., 2011, *Diab Care* **34**: 2279-84. 3) Muller et al., 2012, *Obesity Rev* **13** (Suppl 2): 6-13.