Quantification of total adipose tissue in fetal guinea pigs subjected to suboptimal in utero conditions using water-fat MRI

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Target Audience: Researchers interested in the use of MRI to detect metabolic disease, particularly with respect to its fetal origins.

Purpose: The metabolic syndrome (MetS) encompasses a number of morbidities, including insulin resistance and abdominal obesity, that when presented together increase the risk of developing cardiovascular disease and diabetes.[1] Currently in North America, approximately 25% of the population is afflicted with MetS, a number that is rising.[1] Although MetS is a disease that typically presents itself in adulthood, it has been shown that the propensity to become afflicted with MetS can be established during fetal development.[2] There is an increased incidence of MetS in adulthood for people born within one of two groups: large infants who were over-nourished as fetuses, as well as very small infants that developed within an intrauterine growth restricted (IUGR) environment.[2] It is hypothesized that the altered nutrition of the fetus present in these two cases leads to abnormal fat distributions in the developing fetus. Thus, the goal of this study is to use water-fat separated MRI to image fetal adipose tissue and to identify abnormalities in adipose tissue deposition in these two cases.

Methods: For the current study, pregnant guinea pigs were used due to their similarity to humans in regard to adipose tissue development during fetal growth.[3] Three groups of pregnant guinea pigs were anaesthetized and scanned ~60 days into an ~68 day gestation. These groups included: a high fat diet group where the mother's food consisted of 46% fat by weight; a surgically induced IUGR group on a chow diet; and a control group. IUGR was induced either by vessel ablation or placing an occluder over uterine blood vessels, restricting nutrient and oxygen flow to the fetus. Imaging was performed at 3T (MR750, GE, Waukesha, WI) using a 32 channel receive coil under a protocol approved by the institution's Animal Use Subcommittee. T_1- and T_2-weighted images were acquired with TR/TE/flip angle = 5.1ms/2.4ms/15° and 2000ms/120ms/90°, respectively, with voxel dimensions = 0.875x0.875x0.9mm^3 for both acquisitions. IDEAL water-fat images were also collected for each guinea pig with TR/ΔTE/flip angle = 9.4ms/0.974ms/4° and voxel dimensions = 0.933x0.933x0.9 mm^3. The T_1- and T_2-weighted images were used to locate each fetus and to segment their volumes. IDEAL fat-only images were used to manually segment fetal adipose tissue volumes, and hepatic and intrascapular fat pad fat fractions were determined using proton density fat fraction (PDFF) maps.

Results: Compared to the control group, there was a noticeable difference in hepatic fat fractions of pups born to mothers on a high fat diet (28% vs. 22%), but this difference was not statistically significant (ANOVA, p=0.1). There was however a significant increase in the intrascapular fat fraction of the high fat diet group compared to the control group (84% vs. 77%, ANOVA p=0.01). The proportion of fetal volume comprised of adipose tissue was increased in the high fat diet group (22%), whereas this proportion was decreased in the IUGR (12%) pups compared to the control pups (19%).

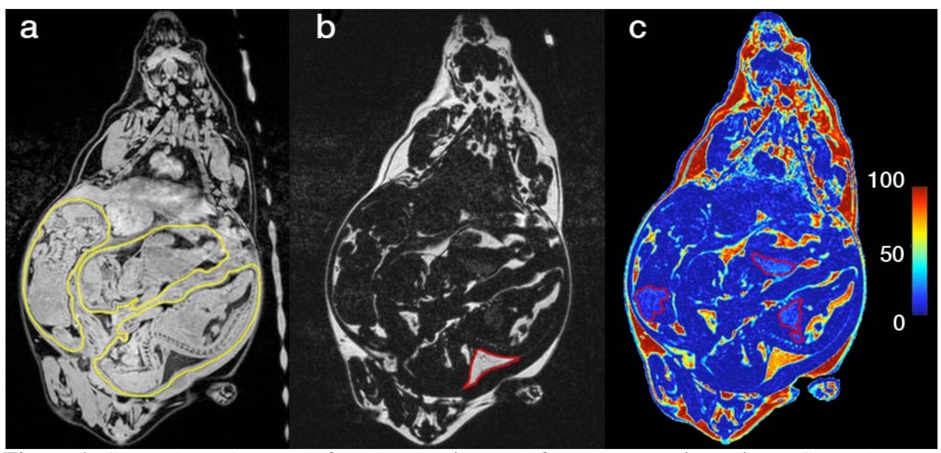

Figure 1: Coronal IDEAL water-fat separated images of a pregnant guinea pig. a) Coronal water only image with fetuses contoured in yellow, b) Fat only image with an intrascapular fat pad contoured in red, and c) Fat fraction map with fat fraction denoted by colour bar and fetal livers contoured in red.

Discussion: The elevated liver fat fraction values in the pups born to mothers on a high fat diet points to early evidence of non-alcoholic fatty liver disease (NAFLD). The increased fetal adiposity of the high fat diet group is also suggestive of NAFLD, but further work must be done to separate the visceral from the subcutaneous adipose tissue in the fetuses. The presence of NAFLD at such an early stage could have a detrimental effect on adult metabolic capabilities. Furthermore, the elevated intrascapular fat fraction in this group signifies a decreased amount of brown adipose tissue, which is characterized by decreased fat fraction due to increased vasculature and mitochondria compared to white adipose tissue.[4]

Conclusions: It is demonstrated here that adipose tissue can be identified and quantified in the fetus. In addition, there is a detectable difference in adipose tissue in pups born to mothers on a high fat diet as well as IUGR pups when compared to controls.

References: 1) Grundy SM. *Arterioscler Thromb Vasc Biol* 2008; 28: 629-636. 2) Brenseke BM, *et al. J Pregnancy* 2013; 2013: 368461, doi:10.1155/2013/368461. 3) Castañeda-Gutiérrez E, *et al. Am J Clin Nutr* 2011; 94(6 Suppl): 1838S-1845S. 4) Hu HH, *et al. Magn Reson Med* 2010; 31(5): 1195-1202.

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