Maternal-fetal exchange and metabolism followed in real-time by dynamic hyperpolarized $^{13}$C imaging on pregnant rats

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The mammalian fetus relies on the placenta to mediate exchanges between maternal and fetal gases and metabolites, and to excrete fetal metabolic wastes. Two thirds of all cases of stillbirth are connected to placental dysfunction. Therefore the ability to non-invasively characterize specific maternal-fetal exchanges by MRI may offer valuable insight to better understand fetal metabolism, developmental physiology and a variety of neo-natal diseases and malformations such as preeclampsia, hyperoxia and hypoxia [4]. This study presents the combination of MRI with dissolution DNP [1-3] to monitor the transport of pyruvate across the placental barrier and its subsequent conversion to lactate in a non-invasive way.

Wistar pregnant rats at late pregnancy stage (embryonic days 17 to 21) were anesthetized with 3% of isoflurane in 1L/min of O₂ and their tail vein was canulated for the injection of hyperpolarized pyruvate. Dynamic $^{13}$C chemical shift imaging (CSI) centric-sampling experiments were performed on a Bruker Biospec 4.7T system using a cross-coil configuration (volume coil transmit / 20mm surface coil receive). A FOV of 5cm and a TR of 68ms was used with a matrix resolution of 12x12 leading to an acquisition time of 8.3s. In addition, T₁ and T₂ weighted $^1$H anatomical images were obtained using gradient- (6.3ms TE, 615ms TR) and spin-echo (29ms TE, 5s TR) sequences with gating. $^{13}$C CSI images were reconstructed with Matlab and each was normalized to the highest intensity.

$^{1}-^{13}$C-pyruvate was mixed with Ox63 (15mM) and hyperpolarized in an Oxford Instruments Hypersense operating at 94GHz and 1.4K. A 3ml bolus of the resulting 80mM hyperpolarized $^{1}-^{13}$C-pyruvate solution was injected into the tail vein of the rat. $^{13}$C CSI were recorded at the end of the injection of hyperpolarized pyruvate or once half of the bolus was injected.

$^1$H anatomical imaging enabled the identification of all key maternal/fetal compartments including the maternal uterine artery, vena cava and the kidneys; the placenta; the fetus and its liver and heart. Series of $^1$-¹³C-pyruvate images recorded with sufficient signal-to-noise ratio (SNR) for over 30s following injection revealed a rapid build-up and decay in the maternal compartments (uterine artery, kidney, vena cava) and the placentas. The conversion of pyruvate to lactate was also monitored by a series of $^{1}-^{13}$C-lactate images. For the maternal kidney a rapid decay of lactate signal is observed. In contrast slow buildup (starting at 16s) and eventual decay (to 56s) is observed in the placentas. This is in accordance with previous data of hyperpolarized urea, which showed slower signal decay after crossing of the placental barrier. In addition, weak, short-lived $^{13}$C-alanine signals were also observed in the fetal livers.

This study proves the applicability of hyperpolarized MRI for studying fetal metabolism in real-time. It may serve as a basis for the potential detection of fetal metabolic conditions such as preeclampsia, hyperoxia and hypoxia.
Figure 1. Overlay of time-trace of $^{13}$C images from injections of hyperpolarized pyruvate with anatomical proton images. Top trace: images of $1^{13}$C-pyruvate. Bottom trace: images of $1^{13}$C-lactate. Placenta 1 (P1), placenta 2 (P2) and maternal kidney (K) are indicated.
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References