

**Title:** Optimizing Hyperpolarized Carbon-13 Magnetic Resonance Imaging of the Placenta using a Hybrid Flip Angle Scheme

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**Structured Abstract:**

**Introduction:** Hyperpolarized magnetic resonance imaging (MRI) of carbon-13 ( $^{13}\text{C}$ ) allows real-time quantitative imaging of key biological molecules, such as pyruvate, and their metabolic processes. We are interested in using this approach as a safe method of examining fetoplacental metabolism in vivo. The hyperpolarized state of pyruvate decays in 20-40 seconds in vivo, leading to issues of low spatial resolution and low signal-to-noise ratio (SNR) in images. Variable flip angle (VFA) schemes have been used to boost SNR by applying a different flip angle for each excitation. We will address the issue of low SNR and practicalities of implementation for imaging by using a hybrid flip angle (HFA) scheme that varies a spectrally selective RF pulse over time.

**Methods:** The HFA scheme produces a different VFA trajectory for each metabolite by progressively varying both the shape and amplitude of the spectrally selective RF shape for each image acquisition, to optimize the signal of each metabolite during the experiment. The pulse shape and amplitude are updated at the beginning of each acquisition and maintained throughout the acquisition. Bloch simulations were used to determine the optimal flip angles for each metabolite using the HFA scheme. Animal experiments were done on two non-pregnant female adult guinea pigs at 3T (Discovery MR750, GE Healthcare, Waukesha, WI) using a custom built  $^{13}\text{C}$  birdcage coil (Morris Instruments, Ottawa, Canada). 3.5 mL of the hyperpolarized 80mM  $[1-^{13}\text{C}]$ pyruvate was injected into the hind leg over 12 seconds. Image acquisition began 7.5 seconds after start of bolus injection and images were acquired every 7.5 seconds. Each animal was scanned with either the HFA scheme or spectrally selective constant flip angles (CFA) previously used in hyperpolarized  $^{13}\text{C}$  imaging studies. SNR was calculated as the mean signal in regions of interest (ROIs) drawn around the kidneys divided by the standard deviation of signal in a noise region.

**Results:** We have shown an in vivo demonstration of a boost in mean SNR provided by an HFA acquisition relative to a CFA acquisition. SNR is most notably elevated at later time points, observing an SNR  $>5$  in the  $>30\text{s}$  after injection range.

**Discussion:** Our in vivo data suggests that the HFA scheme performed better to preserve signal during acquisition compared to the CFA scheme. A higher SNR makes it easier to visualize and quantify results, and is critical for observing metabolism dynamics in the placenta. Future work includes implementing this pulse sequence into our ongoing studies of placental metabolism in normal and growth restricted guinea pig models.