Flow-sensitizing gradients for first-pass perfusion imaging using hyperpolarized 13C urea in the rat heart

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Target. Researchers interested in perfusion imaging and hyperpolarized imaging.

Purpose. Reduced myocardial perfusion results in cell death, reduced contractility, cardiac remodeling, and ultimately heart failure. The infusion of a hyperpolarized contrast agent [1] has long been proposed as a method for perfusion measurement due to the relatively long signal lifetime, low background signal, and linear behaviour of an intravascular contrast agent. While ^{13}C agents such as urea and HP001 have been used as probes of perfusion within the kidneys as well as in cancer [2], application to the heart has been challenging due to the high spatial resolution required. In this abstract, we investigate the feasibility of imaging the first passage of a bolus of hyperpolarized ^{13}C urea through the heart. We propose to use flow-sensitizing bipolar gradients to null the bright signal within the cardiac chambers, enabling direct visualization of the contrast agent within the tissue capillary bed.

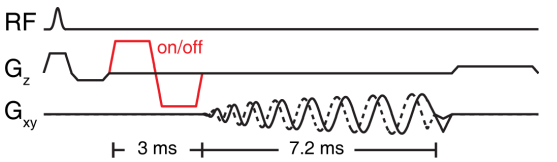

Fig.1. ECG-triggered spiral sequence. The bipolar flow-sensitizing gradient (red) is toggled in alternate TRs, dephasing signal from within the cardiac chambers.

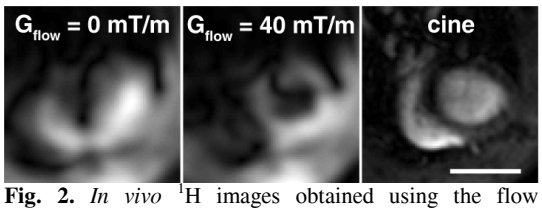

Fig. 2. *In vivo* ^{1}H images obtained using the flow sensitizing gradient. Signal from within the lumen is spoiled, while stationary anatomy is preserved. A cine image is shown as an anatomical reference.

Methods. Pulse sequence. Fig. 1 shows the flow-sensitive, ECG-gated, golden-angle spiral sequence used to obtain axial dynamic ^{13}C urea images in the heart (Agilent 7T, TE 4.7 ms, TR 1 RR, HR ~400 bpm, FOV 20x20 mm^2, acquired in-plane res. 1.25x1.25 mm^2, thk 5 mm, readout 7.2 ms, FA 20°). Flow contrast was incorporated by inserting a bipolar gradient [3] (G_{flow} 170 mT/m, duration 3 ms, orientation through slice direction) between the end of the excitation and the start of the readout. The bipolar gradient amplitude was calibrated by obtaining ECG-gated ^{1}H GRE images (Fig. 2) with the same spatial resolution. The required gradient amplitude to null flowing blood in the chamber was scaled by γ_H/γ_C (approximately four). *In vivo* study. Male Wistar rats (n=4, weight 475 g) were scanned supine using a volume Tx birdcage and 2-channel Rx surface array (Rapid Biomedical). ^{13}C urea (6.4 M) was polarized with a trityl radical (OX63, 15 mM) for 2 hours in a prototype DNP hyperpolarizer, dissolved in 6 mL EDTA, and transferred to a magnetic holder prior to injection. 2 mL of pre-polarized 40 mM ^{13}C urea were injected over 20 seconds via a tail vein. The scan was started prior to injection. Image reconstruction. The multishot spiral trajectory was predicted using a pre-measured gradient impulse response function [4] and the non-Cartesian k-space samples were converted to an image by NUFFT. The images were Hamming filtered to an in-plane resolution of 2.3x2.3 mm^2. A sliding window was used to group spiral interleaves (6 interleaves per image). Data analysis. The heart was manually segmented using the ^{13}C images into right ventricle (RV), left ventricle (LV), and myocardium.

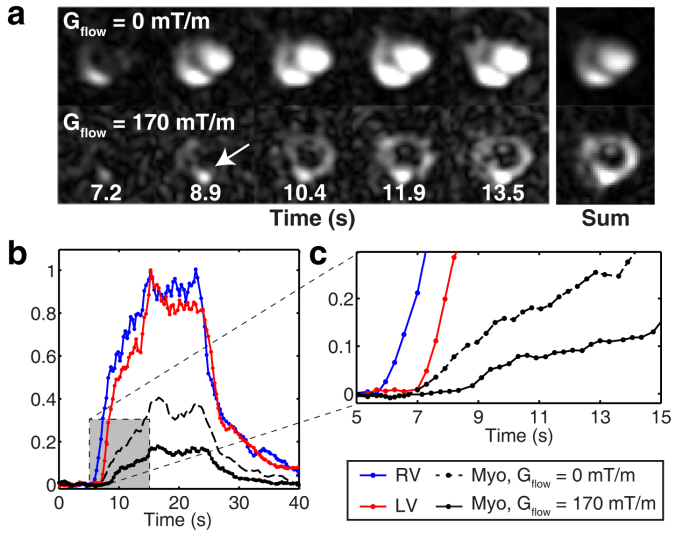

Fig. 3. *In vivo* data showing the first pass of urea in the rat heart. (a) Images from every 5th frame are shown without (G_{flow} = 0 mT/m) and with (G_{flow} = 170 mT/m) flow sensitivity. The arrow indicates residual blood signal in the RV. (b) Time course covering the first pass of the urea signal within the RV, LV, and myocardium, showing (c) the different arrival times of the contrast agent within the compartments.

Results. Fig. 3a shows representative images of the first-pass of the pre-polarized urea bolus through the heart. When the bipolar gradient is off, the myocardial wall cannot be resolved due to insufficient in-plane resolution. The flow-sensitizing bipolar gradient dephases signals within the voxel with varying velocities, enabling direct visualization of the slowly moving ^{13}C urea within the cardiac wall. The time courses (Figs. 3b and 3c) show the different arrival times of the contrast agent within the RV, LV, and myocardium, indicating that the flow suppression reduces contaminating signal from the LV.

Discussion. We have demonstrated that flow-sensitizing bipolar gradients enable direct visualization of slowly moving blood within the myocardium, by nulling flowing signal within the cardiac chambers. Other black blood imaging methods, such as using a spin-echo, are challenging when imaging the first-pass of a pre-polarized agent. In particular, the majority of the ^{13}C label may still be within the transition region of the transmit coil when administered intravenously over 20 seconds. An adiabatic double spin-echo [5] will saturate the ^{13}C signal moving through this region. Alternatively, directly increasing the spatial resolution of the imaging sequence results in a large SNR penalty, and is not feasible due to the high temporal resolution required. We also observe bright signal co-localized to the RV as well as within the lumen of the LV in the flow-sensitized images. As the spoiling efficiency of the flow-sensitizing gradient is related to the velocity distribution within the voxel, these signals are presumably due to insufficient spoiling of slowly moving blood within the chambers. Changing the flow encoding direction from view to view may result in improved flow sensitivity. The sequence can provide multi-slice coverage due to the short TR. In future studies, ^{13}C urea will be used to probe regional changes in tissue perfusion following myocardial infarction. Co-polarization of urea with ^{13}C-pyruvate, and interleaved imaging of the urea resonance may simultaneously provide information regarding myocardial metabolism and perfusion within a single scan.

Conclusions. A flow-sensitized imaging sequence enables imaging of the first-pass of a bolus of hyperpolarized ^{13}C urea through the heart. We anticipate that this probe of myocardial perfusion will enable new applications in hyperpolarized ^{13}C MRI.

References. [1] Ardenkjaer-Larsen JH PNAS 2003 [2] von Morze C MRI 2012 [3] Gordon JW ISMRM 2013 [4] Vannesjo SJ MRM 2012 [5] Cunningham CH JMR 2007