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

1Cardiovascular Medicine, University of Oxford, Oxford, Oxfordshire, United Kingdom, 2Physiology, Anatomy, and Genetics, University of Oxford, Oxford, Oxfordshire, United Kingdom, 3Physics, University of Oxford, Oxford, Oxfordshire, United Kingdom

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 13C 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 13C 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.

Methods. Pulse sequence. Fig. 1 shows the flow-sensitive, ECG-gated, golden-angle spiral sequence used to obtain axial dynamic 13C urea images in the heart (Agilent 7T, TE 4.7 ms, TR 1 RR, HR ~400 bpm, FOV 20x20 mm², acquired in-plane res. 1.25x1.25 mm², thk 5 mm, readout 7.2 ms, FA 20°). Flow contrast was incorporated by inserting a bipolar gradient [3] (Gflow, 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 1H GRE images (Fig. 2) with the same spatial resolution. The required gradient amplitude to null flowing blood in the chamber was scaled by γv/γC (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). 13C urea (6.4 M) was polarized with a trityl radical (OX63, xx 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 13C 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 mm². A sliding window was used to group spiral interleaves (6 interleaves per image).

Data analysis. The heart was manually segmented using the 13C images into right ventricle (RV), left ventricle (LV), and myocardium.

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. In vivo, the urea signal within the RV, LV, and myocardium, showing (c) 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 13C 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 13C 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, 13C urea will be used to probe regional changes in tissue perfusion following myocardial infarction. Co-polarization of urea with 13C-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 13C urea through the heart. We anticipate that this probe of myocardial perfusion will enable new applications in hyperpolarized 13C MRI.