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3D myocardial perfusion quantification using hyperpolarized HP001

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Synopsis

Keywords: Hyperpolarized MR (Non-Gas), Perfusion

We propose a 3D gradient echo sequence with hyperpolarized HP001 as contrast agent for whole heart myocardial perfusion quantification. The estimated perfusion values are correlated with the perfusion values estimated from dynamic contrast enhanced (DCE)-MRI.

Introduction

DCE-MRI using gadolinium (Gd)-based contrast agents is the current MRI standard for myocardial perfusion assessment. Even though Gd-based contrast agents are believed to be safe, concerns about Gd retention in the body have been raised[1]. As an alternative to gadolinium, hyperpolarized ^{13}C urea and HP001(bis-1,1-(hydroxymethyl)-[1-^{13}C]cyclopropane-d8) have been tested pre-clinically for 2D myocardial perfusion assessment[2]. 3D techniques allow for whole heart coverage but are challenging due to low myocardium SNR. This work presents methodology for 3D whole heart myocardial perfusion quantification using hyperpolarized HP001. The method was tested in a pig model and results were compared with DCE-MRI.

Methods

Sequence design

A 3D gradient echo, variable density, stack-of-spirals sequence was designed (see Figure 1) with the following parameters: FOV:150x150x100 mm^3, resolution=3x3x10 mm^3, readout time=21ms. The data acquisition order for phase-encodes was chosen to first acquire odd numbered planes, and then even to enable sliding window reconstruction. The spatial point spread function(PSF) was simulated by performing image reconstruction with all k-space data points set equal.

Coil sensitivity mapping

A home-built ^{13}C 8-channel flexible coil[3] was used for reception and a clamshell type coil for transmission (RAPID Gmbh, Germany). To enable intensity correction for the in vivo experiment, the coil sensitivities were measured using an ethylene glycol phantom, while the coil shape and location was fixed, see Figure 2. A multi-slice 2D spiral GRE sequence with spectral-spatial excitation was used for the sensitivity measurement. B_0 and B_1+ maps were acquired to compensate for reduced signal due to off-resonance and flip angle variations. The measured coil sensitivity map was registered to the ^{13}C in vivo images based on the scanner coordinates.

In vivo experiments

Animal handling

One healthy 40 kg female Danish domestic pig was used in the experiment. Animal handling was as described in reference[4]. Cardiac stress was pharmacologically induced by continuous intravenous infusion(600ml/h) of adenosine(5mg/ml) and dobutamine(12.5mg/ml) in saline. Imaging started 3 minutes into the stress infusion.

Hyperpolarization

Two injections were planned. For each injection, 300uL HP001 with 40 mM trityl radical was polarized with a SpinAligner(Polarize, Denmark). The sample was dissolved into 15 ml saline water, providing 166 mM HP001 solution.

Imaging protocol

All imaging experiments were performed on a 3T scanner(Discovery MR750, GE Healthcare) and all cardiac scans were gated to the diastole.
1. Rest/Stress 13C perfusion images were acquired with: TR/TE=44/1ms, flip angle=10°, rest/stress heart rate=34/54 bpm, image frame time=half cardiac cycle, number of frames=60.
2. Rest/Stress 1H gadolinium inversion-recovery DCE-MRI were performed with: FOV=350x350mm^2, resolution=1.35x1.35mm^2, TI/TE/TR=118/1.12/2.3ms, flip angle=20°, slice thickness=8mm, slice spacing=20mm, number of slices=3, rest/stress heart rate=46/46 bpm, image frame time=1 cardiac cycle, number of frames=64.

Reconstruction

A sliding window approach was used to reconstruct two images from each k-space dataset. Conjugate gradient SENSE reconstruction and intensity correction was performed with the phantom-based sensitivity map. The MIRT toolbox[5] was used for reconstruction.

Perfusion quantification

A constrained decomposition method was used for perfusion quantification for both ^{13}C and ^{1}H data. The method enforces a monotonically decreasing residue function acquired by temporal deconvolution of the myocardial signal with the arterial left ventricle signal.

Correlation study

Perfusion values in stress slice 1 and rest slice 3, see Figure 4, were excluded from the correlation as the DCE-MRI for these slices were wrongly acquired in the systole. The myocardium was divided into 16 segments (Figure 5a), and the correlation of the mean perfusion values for each segment between 13C GRE rest/stress and DCE rest/stress was estimated (22 points in total).

Result and Discussion

The measured polarization levels for the two injections were 23% and 25% at the time of dissolution. The simulated PSF is shown in Figure 1. The measured sensitivity map is shown in Figure 2. Figure 3 shows ^{13}C GRE and DCE image time series. Myocardial perfusion is visible after 9 s. Quantitative perfusion maps are shown in Figure 4. The quantitative GRE stress perfusion estimates are comparable to those from DCE. The ^{13}C GRE rest perfusion estimates are much lower compared to DCE rest. Figure 5 shows correlation (R=0.63) between perfusion estimates by ^{13}C GRE and DCE. Linear regression shows that the perfusion estimates are proportional (k=1), though with a -0.3 ml/g/min offset.

Conclusion

The study demonstrated the feasibility of 3D myocardial perfusion estimation using hyperpolarized HP001 in a pig model. The correlation study shows a correlation(R=0.63) between perfusion values estimated by ^{13}C GRE and DCE-MRI.

## Acknowledgements

No acknowledgement found.

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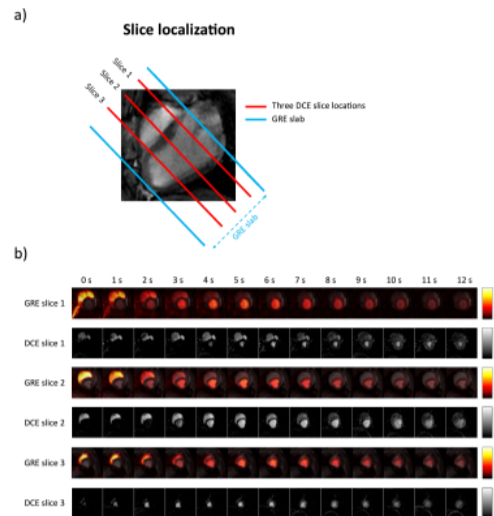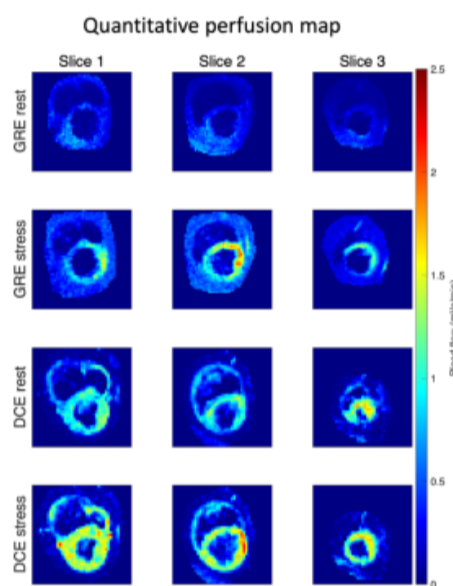
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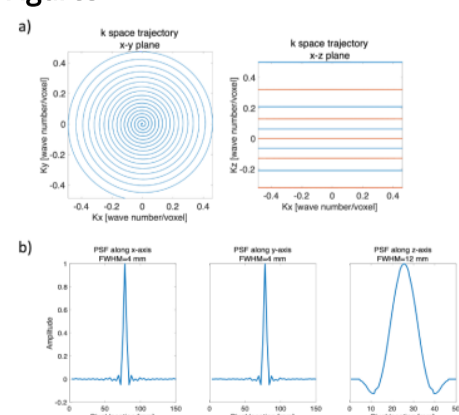
Figure 1: a) Sequence trajectory and b) simulated PSF. An apodization filter is applied to match the k-space density to a Gaussian. The data acquisition was designed to first acquire odd numbered planes (blue), then even numbered planes (orange).
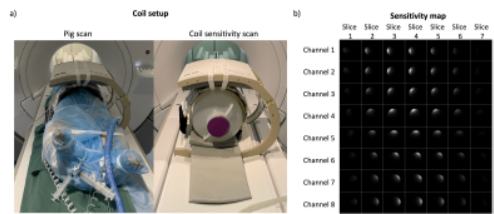

Figure 2. a) Coil setup for in vivo experiment and phantom experiment. The coil shape and position was fixed to keep the coil sensitivity profiles identical between in vivo and phantom experiments. b) measured coil sensitivity maps.

Figure 3. a) Slice locations for DCE and ^{13}C GRE acquisitions. b) Dynamic ^{13}C GRE and ^{1}H DCE imaging. The myocardial perfusion signal is very low compared to the left ventricle and can be seen in the later frames (after 9 s).

Figure 4. Quantitative stress/rest perfusion map estimated by ^{13}C GRE and DCE. The myocardium component is well separated. DCE images have higher SNR. Right ventricle heart wall can be seen in the DCE map but not in the ^{13}C GRE map.
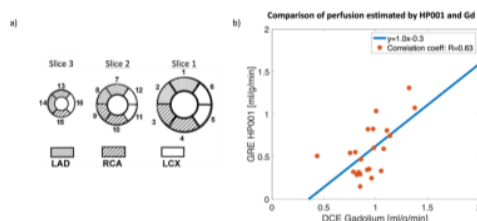
Figure 5. a) Sketch to show the myocardial segmentation. b) Correlation between ^{13}C GRE and DCE perfusion estimates including linear regression and correlation coefficient.