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PET/MRI in the infarcted mouse heart with the Cambridge split magnet

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Abstract

Chronic heart failure, as a result of acute myocardial infarction, is a leading cause of death worldwide. Combining diagnostic imaging modalities may aid the direct assessment of experimental treatments targeting heart failure *in vivo*. Here we present preliminary data using the Cambridge combined ¹⁸FDG PET/MRI imaging system in a mouse model of acute myocardial infarction. The split-magnet design can deliver uncompromised MRI and PET performance, for better assessment of disease and treatment in a preclinical environment.

Keywords

PET/MRI; myocardial infarction; split magnet; mouse

1. Introduction

Acute coronary syndromes represent a leading cause of death in the Western world. When a heart attack occurs, acute ischemia is closely followed by a cascade of events leading to diastolic and systolic dysfunction of the affected myocardium (remodelling), which ultimately lead to the development of heart failure. Novel treatments aim to prevent unfavourable remodelling post myocardial infarction, but it is difficult to observe directly their efficacy.

Current protocols for drug testing in preclinical models of acute myocardial infarction include ex vivo staining techniques targeting specific molecules. Among these, triphenyltetrazolium chloride (TTC) staining, shown in Figure 1, offers a very accurate measurement of infarct size. Histopathology offers very sensitive and specific biomarkers of disease, but the main limitations include impossibility to translate these measurements to clinical trials and to follow-up the disease longitudinally to the chronic stage.

MRI shows structural changes, including remodelling and can be used to measure organ-level functional parameters in addition to tissue perfusion information with gadolinium contrast agents.

PET, with appropriate ligands, can reveal metabolism in the aftermath of insult and show at a molecular level how the heart is responding to treatment.

The main challenge of applying these techniques to the mouse heart is the physical size (about 1 cm in length), pushing the PET to its physical limits in resolution, and the heart rate (450 bpm), representing a challenge for the design of MRI pulse sequences. Significant benefits emerge when the techniques are used together: better time resolution and localisation in PET; comparison of PET tracer images with standard LGE scans.

Here we present early results of cardiac ^{18}F FDG PET/MRI in a mouse model of myocardial infarction with the Cambridge split magnet PET/MRI scanner.

2. Methods

An open-chest mouse (C57Bl/6J) heart model was utilised in which the left anterior descending coronary artery was occluded for 30 min to induce an ischaemic insult. Free access to food and water was given during the period preceding the scans.

A standard cardiac MRI protocol with a 4.7T Bruker BioSpec system was performed 24 h after surgery. Anaesthesia was induced with 3% and maintained with 1.25% isoflurane in oxygen. Temperature was monitored with a rectal probe and maintained constant via a heated water blanket, respiration was monitored using a pillow connected to a piezoelectric transducer. ECG signals were monitored with neonatal graphite (3M) electrodes, placed over the front left and rear right paws.

A 12 cm diameter birdcage was used to transmit the signal and a 2 cm diameter surface coil was used for signal reception. The imaging protocol consisted of scout scans followed by ECG-gated FISP slices (TR/TE 7/2.4 ms 13–20 frames, 3.5 cm FOV, 256 matrix, 1 mm slice thickness, bandwidth 64.1 kHz, FA 20°, 2 NEX), in the long-axis and in the short-axis to cover the whole heart. In post processing, volumes during different phases of the ECG were delineated and integrated over whole heart using Simpson's rule. Global functional parameters were obtained including ejection fraction, the fraction of blood ejected into the circulation during one heartbeat.

After 0.3 mmol/kg intravenous administration of Gadovist, an ECG-gated FLASH IR-sequence was acquired with slices 0.8 mm thick with 0.2 mm gap (FOV 3.5 cm, 256×256, TR/TE 600/2.8 ms, bandwidth 64.1 kHz, FA 60°, 1 NEX). Infarct size was measured by delineating the volumes in the slices and integrating over the left ventricle

After a follow-up period of 4 weeks a second MRI was performed, immediately followed by a combined PET-MRI investigation using the Cambridge split-magnet system [1][2].

The coil used for the PET/MRI experiment was a low pass half-birdcage coil built in house. The capacitors for each leg were taken out of the PET FOV using two strips of thin copper film; tuning and matching circuits were coupled to the extreme legs of the coil. The structure was made of thin plastic to minimize gamma rays attenuation.

The MRI sequence used on the 1T system was a 3D FLASH (0.350 mm isotropic, 256×128×128, TE/TR 6.2/15 ms, BW 50 kHz, FA 15, 6 NEX). The sequence was designed as 3D and isotropic to facilitate post-processing of simultaneous PET/MRI data.

PET imaging consisted of 45 minutes of list-mode acquisition following an intravenous injection of 20 Mbq of FDG. Images were reconstructed using a 3D filtered backprojection algorithm. Images from different modalities were co-registered using affine transformations.

3. Results

Hyperenhancement in the MRI 24 h after the ischemic insult matched a hypointense region of the PET image obtained 4 weeks later, corresponding to a reduced uptake of FDG.

The bright area visible in the LGE scans was reduced in size due to the formation of a scar.

Functionally, there was a decrease in global ejection fraction and a thinner wall in the corresponding scar area, demonstrating the onset of heart failure. In the multimodal simultaneous examination the chambers of the heart are well delineated in both MRI and PET.

4. Conclusions

These preliminary findings clearly demonstrate that the split-magnet design can deliver uncompromised cardiac MRI (albeit low-field) and PET performance. In this study, a very well characterised tracer (FDG) was used, showing correspondence between the different modalities. The results encourage the use of this technique with more complex tracers to target specific molecular pathways, exploiting the better coregistration and anatomical localization. The major benefit of intrinsically co-registered images, compared with histopathology, can improve our understanding of disease and treatment.

Acknowledgments

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6. References

- [1]. Lucas AJ, et al. *Technol Cancer Res Treat*. 2006; 5(4):337–41. [PubMed: 16866564]
- [2]. Hawkes RC, et al. *Technol Cancer Res Treat*. 2010; 9(1):53–60. [PubMed: 20082530]

Figure 1. Slices from TTC staining in a mouse model of acute myocardial infarction. TTC stains in the presence of dehydrogenase enzymes and the non-infarcted myocardium appears brick red.

Figure 2. Sample slices from our Late Gadolinium enhancement protocol.

Following a short delay after the injection of a Gadolinium-based contrast agent the non-viable tissue appears bright and the infarct can be quantified as a percentage of the left ventricle.

Figure 3. A) Long axis and B) Short axis FDG PET-MRI image four weeks after infarct. The reduced uptake of FDG after 4 weeks indicates necrotic tissue in the area pointed by the arrow, this area corresponds to the non-viable tissue 24 hours after I/R injury, shown in C), and D) 4 weeks after injury.