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An isolated pig heart for the development, validation and translation of novel magnetic resonance techniques

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Introduction

Novel magnetic resonance (MR) techniques and imaging biomarkers are often validated in small animal models or empirically in patients. The direct translation of small animal cardiac MR imaging protocols to humans is rarely possible, while validation of novel imaging techniques in humans by tracking changes in MR biomarkers in response to externally controlled changes in blood flow, for example, is difficult, or unethical. An isolated blood-perfused pig heart model which closely resembles human physiology, anatomy and size, can be exquisitely controlled in terms of regional blood flow, oxygenation, afterload and workload, and can be imaged by the same equipment used for humans. It would therefore be a valuable tool for the development, validation and translation of novel magnetic resonance techniques.

Purpose

To design and build a novel MR-compatible, explanted, blood-perfused and free-beating pig heart model and test its feasibility at a clinical 3 Tesla MR Scanner.

Methods

We have designed and built a fully MR-compatible, free beating, blood-perfused, isolated pig heart preparation, capable of being run in an isolated coronary perfusion mode and in working heart mode, providing control of numerous physiologic parameters (see table 1 and figure 1). Hearts were explanted from Large White Cross Landrace pigs (average weight of 50 kg, Harlan Laboratories UK) under terminal anaesthesia and transported to the laboratory under cold cardioplegic arrest (STH solution). The perfusion system consists of a separate haemoperfusate and dialysate circuit. Blood temperature and oxygenation is controlled by an oxygenator with an integrated heat exchanger.

We tested functional cardiac imaging (CINE), high-resolution perfusion imaging (<2 × 2 mm) using a combination of 3 Tesla, parallel imaging (SENSE) and temporal undersampling (kt), as well as late gadolinium enhancement imaging.

Results

The isolated pig heart preparation can be run in the MR environment, with stable physiological function for approximately 4 hours. Image quality was comparable to clinical imaging. Myocardial perfusion imaging was performed at different flow rates including selective intracoronary gadolinium injections. Late gadolinium enhancement imaging was performed in a model of acute myocardial infarction (see figure 2).

Conclusion

The technical design of an isolated pig heart model allows to represent and image in situ cardiac function ex vivo. This novel system allows for excellent control of physiological parameters, validation against gold standards, and easy translation of the methods to patients using the same equipment and imaging sequences.

Figure 1
A Scheme of the isolated perfusion mode. Starting from the perfusate resevoir (38°C) the perfusate is firstly passed through the roller pump 2 into a dialysis module and further through a blood oxygenator with integrated heat exchanger. The oxygenated blood is then pumped into the heart via roller pump 1. Before entering the heart an air trap removes air bubbles from the perfusate. The dialysate (38°C) is pumped through the dialysis module with a centrifugal pump (pump 3, flow of 51 min -1) to exchange metabolites between the venous perfusate and the dialysate. The dialysate is re-circulated in a resevoir. T: sensor for dialysate temperature: O2 and CO2: valves for oxygen and carbon dioxide input. The perfusate resevoir and the venous and arterial blood circiuts are fully water-jacketed. Termperature is controlled by an external heater. **B** Detail of the technical setup of the MR compatible perfusion system. All eletrical parts (control-unit, power-supply, pumps, etc) are placed approximately 6 meters distant to the magenet. The pump engines were then connected to the custom made MR compatible pump heads using polycarbon tubes. **C** Detail Heart Chamber

Table 1: Measurements and Adjustments of physiological parameters in the isolated pig heart model

Parameter	Assessed by	Controlled by	Experimental setup
pO2, pCO2	Oxygen probe (interstitial) Part. Pressure (ven., art.)	Blood oxygenator, oxygenation of dialysate	Levels of pO2: fully adjustable to induce graded hypoxia Levels of pCo2: Adjusted to pH
pH	blood gas analysis	CO2 saturation	Constant
Preload, Afterload	Tip Manometer		Adjustable
CPP, CBF	Tip Manometer, Flowmeter	Flow/Afterload	individually for each coronary
Heart rate	ECG	Pacer	permanent registration
LVP, RVP	conductance catheter, tip-manometer		Constant (Modified according to the afterload level)
Troponin/Myoglobin/Creatine kinase/glucose/lactate	blood samples		Blood Gas Analysis
Tissue	EMB (Histology, immunohisto-chemistry, electron microscopy)		
(CPP Coronary perfusion pressure, LVP left ventricular pressure, RVP right ventricular pressure, SV stroke volume, dP/dt pressure over time/myocardial contractile function, DTF diastolic time frame, EMB endomyocardial biopsy)			

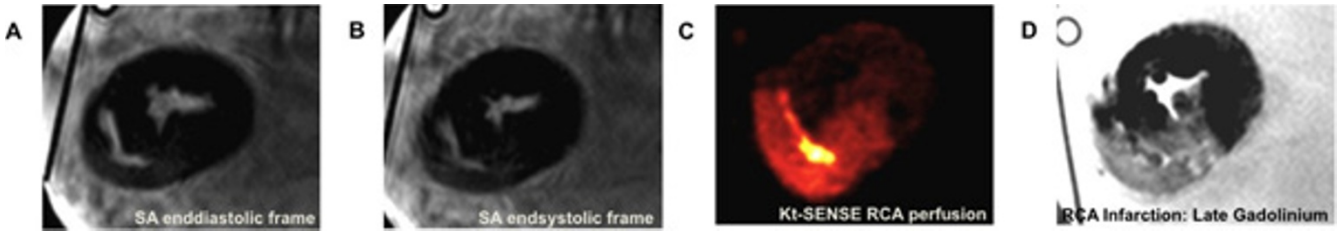

Figure 2
A midventricular short axis view (enddiastolic frame); B midventricular short axis view (endsystolic frame); C kt-SENSE selective Right Coronary Artery (RCA) first pass perfusion (midventricular slice); D Transmural Late Gadolinium Enhancement after 180 munites RCA occlusion indicating myocardial infarction (midventricular slice).