An efficient protocol for infarct quantification in mice

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Target audience

This abstract is directed to researchers working with mouse models of myocardial infarction (MI).

Purpose

To assess myocardial viability following infarction, late gadolinium enhancement (LGE) after injection of a contrast agent is used[1]. While protocols for performing this procedure in humans are established, the different heart rate in rodents mean that different approaches must be employed and there is still uncertainty about the best method to use. For instance, a recent study from Protti *et al*[2] has shown that in mice, TI-optimised standard IR FLASH does not perform better than a cine-MRI sequence without preparation at 7T. To overcome these problems, Price *et al*.[3] have proposed a TI-optimised LGE protocol for rodents based on a fast multi-slice approach. Building on the work of Price *et al*[3], our acquisition strategy relies on acquiring multiple slices in a single heartbeat and interleaving slice groups in alternate TRs using a fixed TI at 4.7 T.

Methods

Phantom experiments To select the parameters for our *in vivo* sequence we modelled healthy and infarcted tissue with 7 vials containing varying concentrations of Gadovist in water. Three vials were chosen to model healthy tissue (T1>0.5 s) and four for a range of potential pathological enhancements (T1<0.5 s). We imaged using the same sequence used *in vivo* with a fixed TI (280 ms) and a range of flip angles (10°-90°) and TR (350-1550 ms).

In vivo imaging protocol Reperfused myocardial infarction was induced in male mice (age 8-10 weeks) with the procedure described in Methner *et al*[4]. Twenty-four hours later, mice were induced with 3% isoflurane in 1l/min O_2 and maintained in anaesthesia with 1.5% isoflurane in 1l/min O_2. After standard long and short axis cine imaging (Cine-FISP: 3.5 cm FOV, 256x256 matrix, TR/TE=7/2.3 ms FA: 20˚, 2 NEX, duration: 1 minute), LGE imaging was performed. After administration of 0.3 mmol/kg Gadovist i.v., an IR-sequence was acquired with slices 0.8 mm thick with 0.2 mm gap, covering the whole heart (FOV 3.5 cm, 256x256, TE/TR 2.8/550-750 ms depending on heart rate, FA 60˚, selective inversion slices, sech shape pulses of 5ms duration, 0.8mm thick, 1 NEX). The duration of the whole protocol (from the start of the anaesthesia to the end of the MRI) was 35 minutes.

Inversion recovery sequence Acquisitions were ECG gated but not respiratory gated. The scheme for our inversion recovery sequence is shown in Figure 1. A delay followed each trigger such that after an inversion time TI, the images would be acquired in end-diastole. Slices are acquired in two groups in alternate TRs so that there is sufficient time for T1 recovery following inversion.

Viability assessment Infarcts were manually delineated on the IR images while the whole LV was segmented on the cine images. Hyperenhancement was measured at three locations in all mice (n=35). Six mice were sacrificed immediately after the protocol, the heart was extracted, cut in 1-mm thick slices and stained with triphenyl tetrazolium chloride (TTC).

Results

In our phantom experiment, we found that with TR between 550-750 ms, optimal CNR was achieved with and a fixed TI of 280 ms, and a FA of 60°. Hyperenhancement (% elevation) was at least 200% in every case, those parameters were therefore chosen for our *in vivo* sequence. Our *in vivo* protocol confirmed this result obtaining a hyperenhancement of at least 200% (apex 404±44, mid-ventricle 580±62, base 540±55, percentage mean ± SEM, one slice per location, n=35) between infarcted and remote tissue for all the mice examined. Intervals for heart rate were 400-500 bpm, respiration rate 30-45 bpm. We did not observe motion artifacts in any of the images and found that a TI of 280ms worked well for each mouse. Bland-Altman and correlation plots revealed excellent correlation between MRI and TTC without a marked bias (See Figures 2 and 3).

Discussion and Conclusions

Using phantom experiments we identified sequence parameters (TR and FA) for a good hyperenhancement and CNR with a fixed TI. Measurement of hyperenhancement *in vivo* in a large cohort and comparison with TTC staining proved that our LGE sequence for mice achieved high quality images in excellent agreement with histology. The protocol is easy to implement and does not require an additional sequence for TI optimization. In the context of drug testing in MI, a fast and efficient protocol is important for greater throughput and reduces mortality and adverse effects of anaesthesia.

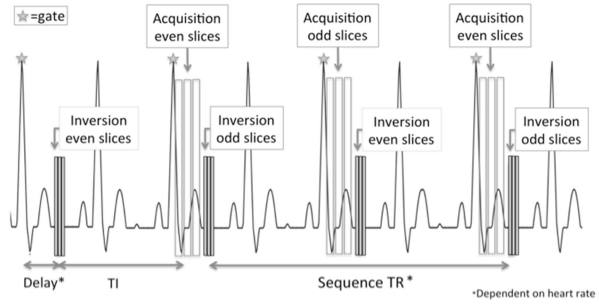

Figure 1: The acquisition scheme of our inversion recovery sequence.

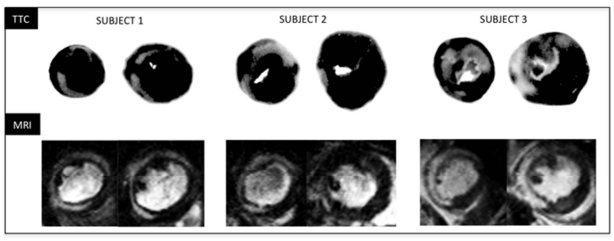

Figure 2: Comparison between TTC staining and LGE MRI.

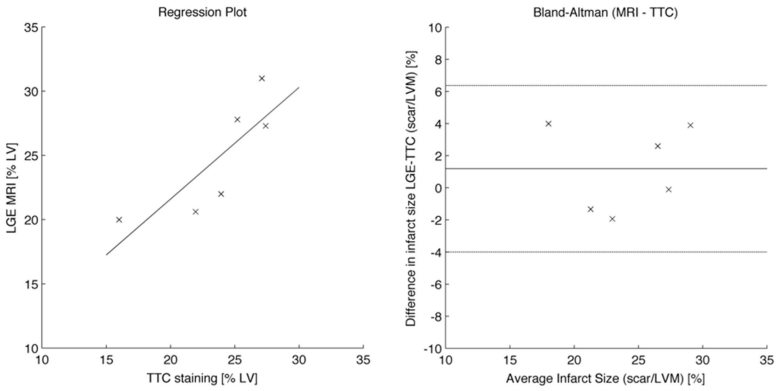

Figure 3: Correlation (slope=0.87, intercept=4.2, r2=0.67) and Bland-Altman plot comparing TTC staining and LGE MRI.

References [1] Simonetti *et al.* Radiology 2001;218:215-223; [2] Protti *et al*. J Magn Reson Imaging 2010;32:878-886; [3] Price *et al.* J Cardiovasc Magn Reson 2011; 13:44; [4] Methner *et al.* Am Jour Phys Heart and Circ Phys 2010;229:H1262-1264