# MRI OF RAT'S HEART AND T1 QUANTIFICATION

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**Abstract**: This paper is focused on developing a retrospective gating algorithm for rat heart MRI and T1 quantification. The first goal is to develop an algorithm binning acquired echo signals according to the corresponding phases of the cardiac and respiratory cycles. The echo signals are acquired using an inversion-recovery 2D gradient-echo sequence with radial encoding and golden-angle increment of the k-space trajectory in the read-phase directions. The next goal is compressed-sensing reconstruction of images. The third goal is fitting a T1-relaxation model to the reconstructed images to obtain quantitative T1 maps.

**Keywords**: rat, heart, cine, MRI

## 1 INTRODUCTION

Magnetic resonance (MR) cardiac imaging is quite challenging due to cardiac and respiratory motion. To obtain clean imaging some form of synchronization/gating is required. The standard clinical procedure usually incorporates prospective gating of acquisition with respect to a measured electrocardiography (ECG) signal. With some sequences, this is not easily done due to the induction of electric current in the ECG leads, which can make successful ECG gating harder or near impossible, especially with small-animal heart imaging and high-field MR systems. Because of these limitations, methods for retrospective self-gated acquisition have been proposed.[1] [2]

These methods are usually based on some form of navigator acquisition, either from within the imaged slice or from a separate navigator slice. This work is focused on MRI methods for quantification of myocardium T1 in small animals (mice, rats). For small-animal MRI, dedicated methods have to be used because of much faster cardiac and respiratory activity, compared to humans, and because of the impossibility of breath-hold acquisition typical for clinical cardiac MRI.

The images can be further processed into T1 relaxation maps, which can serve as an early marker of several diseases. We can use for example two T1 maps measured before and after contrast-agent administration to estimate the ECV (Extracellular fractional volume), which serves as a marker of fibrosis. [4]

For T1 quantification, 2 main methods are usually used: so-called VFA (Variable flip angle)[2] and IR (Inversion recovery)[1]. The VFA mapping is very sensitive to inhomogeneities of the B1 field (present especially in high-field MRI), because of this we focus on IR sequences.

To the author's knowledge, the only IR method for small-animal cardiac quantification of T1 maps with retrospective gating is 2D inversion recovery acquisition in [1], which cannot detect respiratory and cardiac phases close to the point when the magnetization crosses zero during its recovery towards the steady-state following the IR pulse. Furthermore, the method needs long waiting periods between the end of the pulse train and following inversion pulse, due to the usage of simple T1 quantification model and external respiratory synchronization to start the inversion cycle at the same respiratory phase which elongates the acquisition time.

The method proposed in this paper solves these two problems. It provides reliable cardiac and respiratory synchronization also around the zero-crossing points without the need for external sensors and since we use a more complex model, we can eliminate the waiting periods.

## 2 MATERIALS AND METHODS

The proposed method uses a 2D gradient-echo acquisition scheme with radial readout as in [1]. A navigator signal consisting of the first point of every FID (Free induction decay) signal is extracted from acquired data. Since we use an inversion recovery sequence the navigator depends not only on cardiac and respiratory motion but also on the recovery of the magnetization of blood and tissues to their steady state after being inverted by an IR pulse. This multi-exponential recovery trend has to be eliminated from the navigator signal first. To achieve this, the data points are reordered with respect to their position in the IR-IR interval (an interval between consecutive IR pulses) and fitted with a polynomial of the 8th degree, such a high degree is mandatory in order to cover the fast recovery at the beginning of the inversion period. Usually, no regularization is needed as this fit is performed on all data at once (roughly 80000 points for a 10-minute long acquisition). A set of simple bandpass FIR (Finite impulse response) filters is then applied to extract the base frequency bands of the cardiac and respiratory activities. The resulting cardiac and respiratory navigator signals are then fed through a one-way zero-cross detector to form timestamps marking each period. As mentioned in the introduction, the timestamps around the magnetization's zero-crossing points cannot be reliably estimated. To do this the mean cardiac and respiratory periods between acceptable timestamps are computed and the missing data are then interpolated assuming constant cardiac or respiratory rates. For respiratory navigation this serves as a starting point from which every interpolated point is then shifted to the largest local maximum of the original navigator signal, to compensate for irregularities in the breathing cycles and mark the inspiration phase. The interpolated heart timestamps are kept at the interpolated values since, the heart rate usually does not change much within the inversion cycle.

After this interpolation, the timestamps are used to bin the acquired echo signals according to their cardiac and respiratory phases. Binning the data with respect to the current length of the heart or breath period ensures that even if the heart rate changes, the same fraction of the period i.e. the same image is always reconstructed, which further reduces artifacts in the image. The binned echo signals are then used in compressed-sensing iterative image-sequence reconstruction, including regridding of the measured data points from the polar to the Cartesian system (required for radial sampling acquisition methods) and Total variation regularization applied both in the spatial as well as temporal (Inversion recovery) dimensions.[5]

Quantification of T1 is based on the Inversion recovery Look-Locker model, where one inversion pulse is followed by a train of readout pulses. This model includes the effect of the excitation pulses of the sequence.[6]

To validate the proposed methods a preliminary study on rats with induced diffuse myocardial fibrosis has been conducted. Four rats were examined in 2 time points, one before any treatment and one following 14 days of the fibrosis-inducing treatment. Two of the rats served as controls and two rats were induced myocardial fibrosis according to [3]. The animal model was implemented at the Department of Physiology of Faculty of Medicine at Masaryk University. The MRI examination took place at the Institute of scientific instruments of the Czech Academy of Science in Brno using the Bruker Biospec 94/30 9.4T NMR spectrometer. The procedure consisted a of series of scans focused on anatomical features, mainly the ejection fraction estimation and then the precontrast and postcontrast measurement of T1 relaxation maps using the proposed radial sequence. Contrast agent (gadopentetate dimeglumine [Magnevist]; Bayer-Schering AG, Berlin, Germany) was administered. The dose was computed according to the examined rat weight (0.2 mmol/kg) and was intravenously administrated as a bolus between the precontrast and postcontrast acquisitions. The pre- and post-contrast T1

measurements were done in a single short-axis slice with the following parameters: TR/TE= 7.5/1.7 ms, IR-IR interval: 11.25 s, matrix 128x128, adiabatic IR pulse. The resulting T1 maps were then used to calculate the ECV according to [4].

## 3 RESULTS

The proposed methodology was evaluated with respect to synchronization, perceived quality of the reconstructed T1 maps and the consistency of the resulting ECV values. The quality of synchronization can be supported by the analysis of the gating results. This analysis consisted of manual annotation of four 10-minutes long acquisitions acquired from healthy rats and comparison with the automatic detection of respiration. The result was an F1 score of 99.5 %. A similar evaluation of the cardiac gating was not possible because the cardiac navigator shape is not used for synchronization (only its base frequency), therefore a timestamp is guaranteed in every cardiac cycle, furthermore an ECG acquired during the acquisition would be too noisy, as expected for small animals and a high-field MR scanner.

The resulting T1 maps (example in Figure 1) showed a good spatial consistency with clear outlines of the cardiac structures and homogeneous myocardium areas. The pre- and post-contrast T1 values evaluated within hand-drawn myocardium regions of interest and for each examination of each animal were converted to ECV values. The boxplots in Figure 2 show the calculated ECV values for F (Fibrotic) and C (Control) subjects at the beginning of the experiment and 2 weeks after the treatment.

For fibrotic myocardium, the ECV is known to be higher than for a normal myocardium tissue. The significance of ECV increase was evaluated by paired single-sided t-test with a null hypothesis that the ECV values did not change and an alternative hypothesis that the ECV values with the fibrotic specimen have increased. The resulting p-value of the fibrotic group of $2.48 \cdot 10^{-120}$ strongly supports the alternative hypothesis, indicating that the proposed methodology can measure elevated ECV in fibrotic myocardium.

For a more sound conclusion, hematocrit (HCT) should be measured at each MR examination, as the ECV values, as calculated from the T1 maps, are weighted by a factor including HCT. Since the ECV values decrease with the healthy group, it is probable that the fibrosis must even strongly counteract this trend caused probably by animal growth and possibly HCT fluctuation.

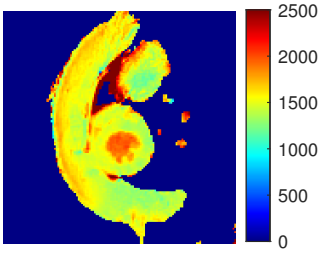


**Figure 1:** Example of one short axis slice of precontrast T1 map

## 4 CONCLUSION

We have proposed a set of acquisition and processing methods that might give reliable estimates of myocardial T1 and ECV which are important biomarkers characterizing fibrosis. The conducted preliminary study has shown significant changes in ECV in the fibrotic group ($p < 0.05$). More conclusive results will be obtained when more animals are included in the study, which is the aim of our follow-up work, together with including measurements of HCT.

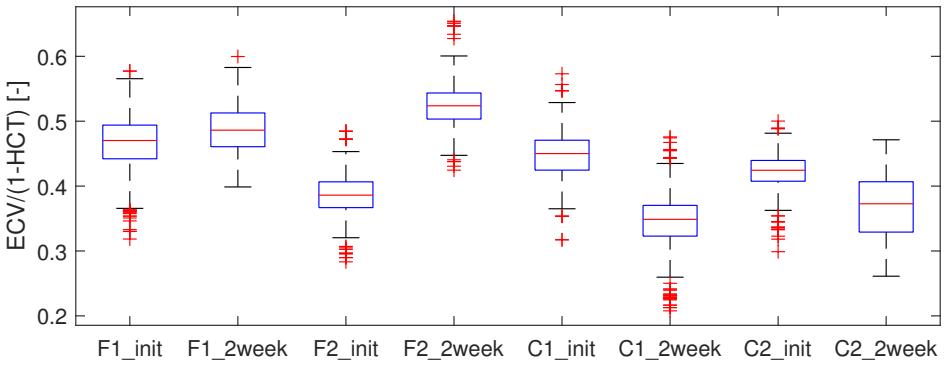


**Figure 2:** Resulting ECV/(1-HCT) values. F (Fibrotic), C(Control)

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