

# Exercise Cardiac MRI, a Clinical Reality with Compressed Sensing

Wendy Strugnell, BAppSc(MIT) FSMRT; Aaron Lin, MBChB, FRACP

Richard Slaughter Centre of Excellence in Cardiovascular MRI, The Prince Charles Hospital, Brisbane, Australia

## Introduction

Non-invasive assessment of ventricular function plays an important role in the diagnosis and management of cardiac diseases. With its high temporal and spatial resolution, cardiac MRI is considered the most accurate non-invasive tool for providing left ventricular (LV) volumes, ejection fraction (EF) and mass at rest [1-3]. Cardiac MRI is also superior to other imaging modalities for quantitative assessment of the complexly shaped right ventricle (RV) [4-6].

Due to practical and technical limitations of imaging, clinical cardiac assessment is conventionally performed with the patient at rest. However, in many heart diseases, symptoms do not occur at rest and ventricular assessment during exercise is necessary to unmask ventricular dysfunction that is not apparent at rest. Despite recent technological advances across imaging modalities, assessment of dynamic ventricular

response during exercise remains challenging. Until now, non-invasive quantitative cardiac assessment during exercise has been performed using echocardiography and nuclear scintigraphy, both of which have significant limitations, particularly in the assessment of the RV. As MRI is superior to other imaging modalities in accuracy and reproducibility of ventricular functional results at rest, there is a clinical need for a reliable MRI assessment of the heart during exercise.

## Limitations of cardiac MRI during exercise

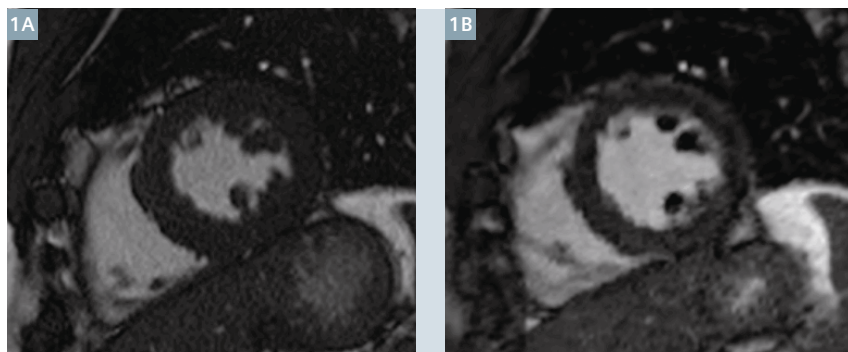
Quantitative MRI assessment of cardiac function requires the acquisition of a stack of ECG-gated, cine ventricular short-axis images [5]. This time-consuming process requires multiple breath-holds to cover the entire ventricle and can be difficult for some patients to complete. This process can be made more

challenging by exercise, particularly in patients with cardiac and pulmonary diseases whose baseline exercise and respiratory capacities are limited.

These limitations have driven the search for faster imaging techniques that maintain acceptable image quality and temporal resolution from resting heart rates through to accelerated heart rates during exercise. Real-time MRI is less susceptible to motion caused either by exercising or breathing and can be performed without ECG gating. La Gerche et al. [7] recently demonstrated that when real-time ungated MRI is combined with *post hoc* analysis incorporating compensation for respiratory motion, accurate biventricular volumes could be measured during maximal exercise. However, the methodology is labor intensive with lengthy post-processing times, and the authors acknowledge that there is significant difficulty in identifying the endocardium at higher levels of exercise. Access to commercially available processing software to enable analysis is another major limitation of this technique. Most real-time sequences also have low temporal resolution, which may affect accuracy at the high heart rates encountered during exercise. Clearly, the pursuit for a fast, clinically feasible MRI technique for evaluating the ventricles during exercise remains.

## Compressed Sensing MRI

Compressed Sensing (CS)<sup>1</sup> was recently proposed as a means to considerably



**1** Midventricular short-axis images at end-diastole from the conventional bSSFP acquisition (acceleration factor 2) (**1A**) and the high spatial and temporal resolution CS\_bSSFP acquisition (acceleration factor 8) (**1B**), from the same patient.

<sup>1</sup> 510(k) pending. Compressed Sensing is not commercially available. Future availability cannot be guaranteed.

accelerate data acquisition through sparse sampling and reconstructing signals or images from significantly fewer measurements than were traditionally thought necessary [8, 9]. Using incoherent sparse sampling, nonlinear reconstruction algorithms and iterative processing, these methods reconstruct undersampled data from significantly fewer measurements whilst maintaining in-plane spatial resolution [10]. Cardiac MRI is ideally suited to CS techniques. Vincenti et al. [11] demonstrated that the application of CS to cardiac imaging enabled several-fold acceleration and achieved a cine acquisition of the whole heart in one breath-hold.

With local institutional review board approval, we recently tested a prototype, ECG-triggered balanced steady-state free precession cine sequence with compressed sensing (CS\_bSSFP)<sup>1</sup> (net acceleration of 8) against the conventional bSSFP sequence (net acceleration of 2) on clinical patients using comparable parameters for spatial and temporal resolution. We concluded that accurate and reproducible volumetric quantifications equaling those of conventional bSSFP could be achieved in the assessment of the left ventricle at rest in various cardiac disease states at significantly shorter acquisition times [12] (Fig. 1).

	bSSFP	CS_bSSFP <sup>1</sup>
TR (ms)	3	2.53
TE (ms)	1.25	1
Field-of-view (mm)	380 x 290	380 x 312
Image Matrix	304 x 232	192 x 192
Spatial resolution (mm)	1.25 x 1.25	1.98 x 1.98
Temporal resolution (ms)	~30	~20
Slice thickness/gap (mm)	8 mm / 2 mm	8 mm / 2 mm
Flip angle (°)	70	70
Bandwidth (Hz/pixel)	914	898
Heartbeats per slice	14-20	1 or 2*
Cardiac phases	30	18-25*
ECG triggering	Retrospective	Prospective
Breath-holds	10	1 or 2*
Breath-hold duration (s)	10	5-7*

\*Heart rate dependent

**Table 1:** Imaging parameters of conventional bSSFP and CS\_bSSFP<sup>1</sup> sequences.

## Exercise cardiac MRI

Patients with cardiac and pulmonary diseases typically have limited exercise tolerance and breath-hold capacity. Quantitation of ventricular function by cardiac MRI during exercise requires:

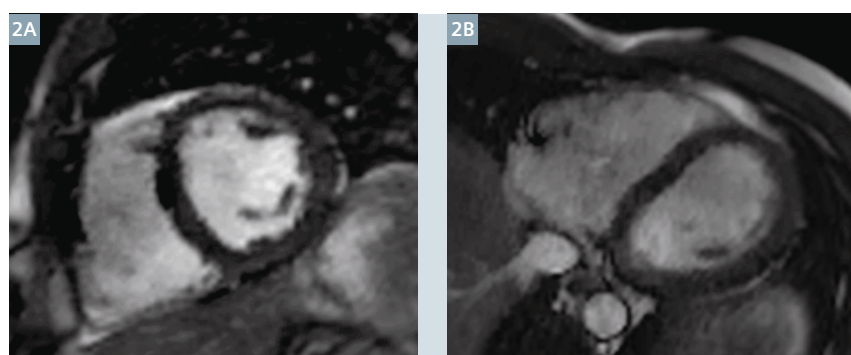
1. Fast acquisition covering the whole ventricle to avoid fatigue from exercise (maximum total exercise time 15 minutes);
2. Short duration of breath-holds to improve patient compliance and to minimize heart rate recovery during suspension of exercise;
3. ECG gating to enable segmented data in discrete cardiac phases for ventricular analysis using commercially available software;
4. Acceptable spatial resolution to delineate ventricular borders for analysis; and
5. Sufficient temporal resolution for accurate determination of end-diastole and end-systole at high heart rates.

To meet all the above requirements, the prototype CS\_bSSFP protocol was modified for use under exercise conditions. Typical imaging parameters are given in Table 1. A net acceleration factor of 11.5 was achieved which enables whole heart coverage in one or two breath-holds (5-7 s duration depending on heart rate), with in-plane spatial resolution of 2 mm<sup>2</sup> and temporal resolution in the order of 20 ms. CS\_bSSFP images in the LV short-axis (SAX) and modified RV SAX [13] are shown in Figure 2.

## Exercise MRI protocol

### Pre-MRI exercise testing

Prior to the exercise cardiac MRI, a cardiopulmonary exercise test (CPET) is performed outside the MRI room using a portable metabolic system (Metamax, Cortex BXB, Leipzig, Germany) and an MRI cycle ergometer (Lode, Groningen, The Netherlands). The maximal workload achievable by the patient is determined and then used to calculate the sub-maximal workloads for exercise cardiac MRI. Typically, this is between 25-60 W.



**2** Midventricular LV short-axis and modified RV short-axis images from the highly accelerated CS\_bSSFP acquisition (net acceleration 11.5) at end-diastole from the same patient.

During CPET, the patient is coached by the physiotherapist to hold their breath without valsalva breathing. This is to reduce the potential for intra-thoracic pressure increasing during breath-hold, which in turn could cause reduced venous return and cardiac output.

### MRI protocol

After a recovery period, the patient is positioned in the MRI scanner (1.5T, MAGNETOM Aera). ECG and blood oxygen saturation (SPO<sub>2</sub>) monitoring is used throughout the examination under the supervision of a cardiologist. After cardiac localizers are obtained, both LV short axis and modified RV short axis stacks are acquired at rest and two pre-determined submaximal workloads (Rest: 0 W, Exercise 1: 25 W and Exercise 2: 40-60 W). In order to achieve steady-state exercise response, subjects cycle at each workload for 3 minutes prior to image acquisition. Between breath-holds, subjects resume cycling for 45 s to return to steady-state exercise response (Fig. 3).

### Exercise MRI Analysis

Image analysis is performed off-line using cvi<sup>42</sup> software (Circle Cardiovascular Imaging, Calgary, Canada) and all standard measurements of cardiac function are obtained.

### Clinical feasibility

In pilot testing, we demonstrated that this exercise MRI protocol is feasible in patients, healthy controls and in well-trained athletes, with clinically acceptable image quality (Fig. 4). Exercise ergometry within the MRI scanner is well tolerated and breath-holds during image acquisition are achievable at submaximal exertion. Quantitative ventricular data and dynamic ventricular response during exercise can be determined using the ultrafast prototype CS\_bSSFP sequence.

### Clinical applications and potential

Insights from analysis of pressure-volume loops have demonstrated that a ventricle that adapts well is able to increase its contractility to match the chronic increase in afterload and

its preservation is important in maintaining ventricular efficiency [14]. Ventricular systolic function adaptation to afterload can be tested dynamically to determine a contractile reserve, the capacity to increase contractility at a given level of loading. Contractile reserve has been shown to be a strong prognostic predictor in patients with left heart failure [15].

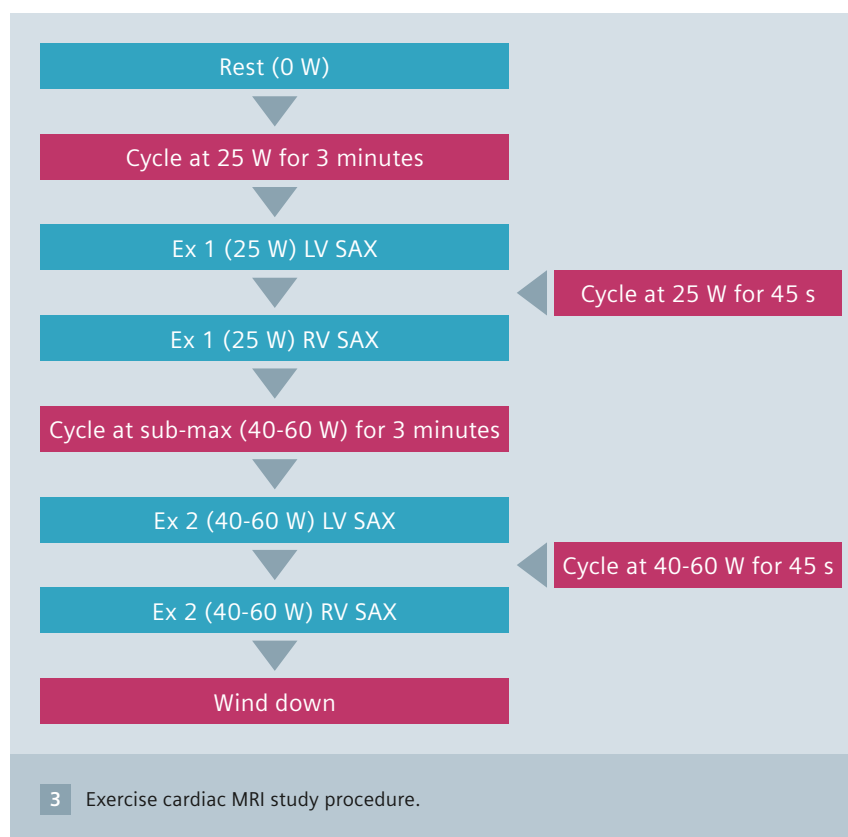
Assessment of RV function during exercise may provide an early indication of RV dysfunction and add incremental value in the clinical assessment of patients with right heart disease. In the setting of a chronic pressure overload state such as in pulmonary arterial hypertension (PAH), RV contractile reserve may be a more sensitive marker of hemodynamic ventricular dysfunction.

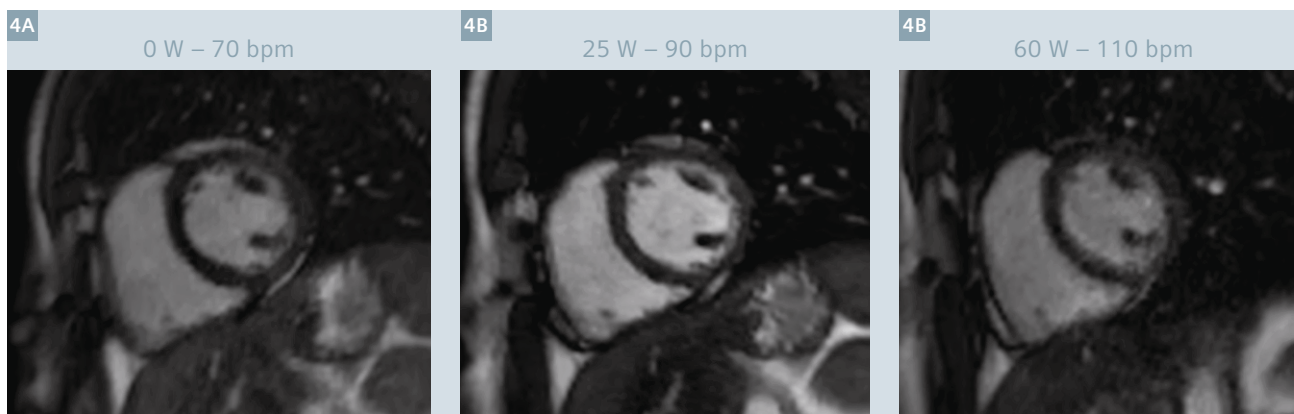
Currently, there is limited data on RV function during exercise and RV contractile reserve, largely due to the limitations of imaging during exercise. In a small study of pulmonary arterial hypertension (PAH) patients and normal controls, we demonstrated that although having near-normal ventricular function at rest, PAH patients were unable to increase their RV contractile function during exercise [16] (Fig. 5).

Exercise MRI also has the potential to predict adverse surgical outcomes in patients with congenital heart disease undergoing valve replacement surgery. The surgical outcome is likely to be better in patients with a ventricle shown to have contractile reserve. Exercise MRI may enable better-informed decisions about the timing of surgical and therapeutic interventions by detecting early ventricular impairment during exercise (particularly in the right ventricle). By providing information on ventricular contractile reserve, exercise MRI may facilitate improved prognostication of patients and has the potential to predict adverse surgical outcomes.

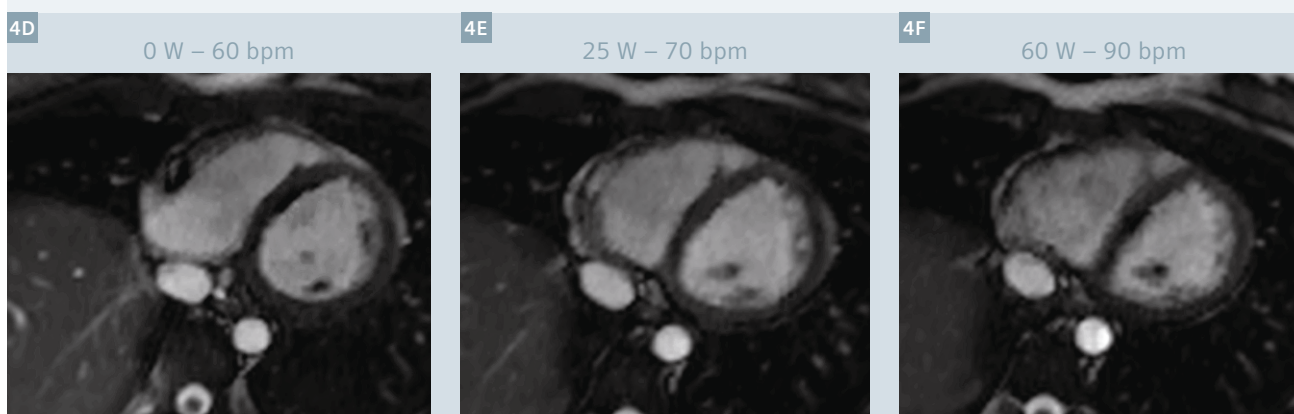
### Conclusions

We have demonstrated that a highly accelerated imaging sequence using compressed sensing can facilitate clinically useful dynamic assessment of biventricular response during exercise with a reliability that was not previously possible.

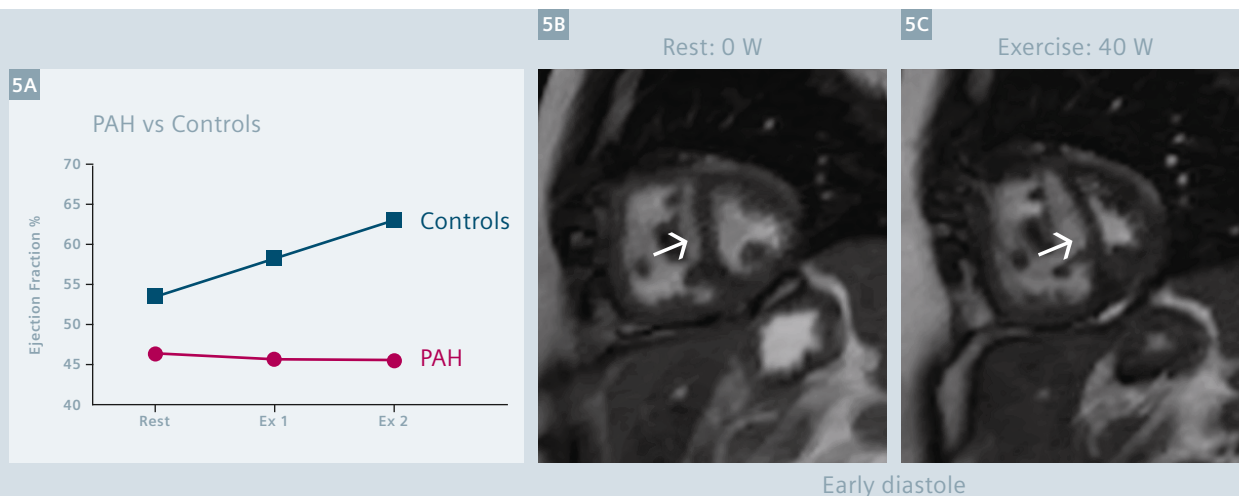




**4A-C** Midventricular LV short-axis images at rest and two submaximal workloads at end-diastole using the CS\_bSSFP acquisition in a male control.



**4D-F** Midventricular modified RV short-axis images at rest and two submaximal workloads at end-diastole using the CS\_bSSFP acquisition in a female control.



**5** **5A:** Exercise MRI unmasks RV dysfunction not evident at rest in patients with pulmonary arterial hypertension (PAH): Despite having near-normal RV function at rest, PAH patients were unable to increase their RV contractile function during exercise.

**5B, C:** Midventricular LV short-axis images showing a left-ward deviation of the interventricular septum in early diastole during sub-maximal workload in a pulmonary arterial hypertension patient.



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## Contact

Ms Wendy Strugnell  
Richard Slaughter Centre of Excellence in  
Cardiovascular Magnetic Resonance Imaging  
The Prince Charles Hospital  
627 Rode Rd  
Chermside QLD 4032  
Australia  
Phone: +61-7-3139 6849  
wendy.strugnell@health.qld.gov.au



Wendy Strugnell



Aaron Lin