Cardiovascular magnetic resonance in patients with cardiac resynchronisation therapy: Is it time to scan with resynchronisation on?

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Abstract

Cardiac resynchronisation therapy is recommended in international guidelines for patients with heart failure due to important left ventricular systolic dysfunction (or HEFREF) and ventricular conduction tissue disease. Cardiac magnetic resonance (CMR) represents the most powerful imaging tool for dynamic assessment of the volumes and function of cardiac chambers but is rarely utilised in patients with CRT due to limitations on the device, programming and scanning. In this review we explore the known utility of CMR in this cohort with discussion of the risks and potential benefits of scanning whilst CRT is active, including a practical strategy for conducting high quality scans safely. Our contention is that imaging in patients with CRT could be improved further by keeping resynchronisation therapy active with resultant benefits on research and also patient outcomes.

Key words: Heart failure, cardiac resynchronisation therapy, cardiac magnetic resonance,

Introduction

In addition to survival benefits, cardiac resynchronisation therapy (CRT) can improve symptoms and functional capacity in patients with left ventricular systolic dysfunction and conduction delay [1-3]. Consequently CRT has a class 1a level of recommendation in both European and American guidelines for symptomatic patients with prolonged QRS duration on ECG and severe left ventricular systolic impairment [4, 5].

Cardiovascular magnetic resonance (CMR) is accepted as the gold standard imaging modality for assessing cardiac volumes, mass and ejection fraction [4]. CMR also has an important role in the assessment of myocardial fibrosis, ischaemia and viability. The pattern of scarring can be helpful in differentiating the aetiology of heart failure including ischaemic or dilated cardiomyopathy. CMR can also contribute to the diagnoses of rarer conditions such as myocarditis, sarcoidosis and haemochromotosis. In most of these diseases, the extent of scarring also provides powerful prognostic information [6]. There are no data to describe the rate of use of CMR in CRT patients either for follow-up or for the diagnosis of other cardiovascular and non-cardiovascular problems, but we expect this is very low.

The advent of magnetic resonance (MR) conditional pacemakers and devices could offer the exciting opportunity to assess specifically the effect of biventricular pacing on cardiac volumes and function using the most reproducible imaging technique. Indeed the recent joint statement from the British Cardiovascular Society and the Clinical Imaging Board indicates the safety of using CMR in device patients [7].

However, the majority of devices disable left ventricular pacing when put into the CMR-scan mode. Thus, the images obtained are limited by dyssynchrony associated with the intrinsic underlying conduction delay or right ventricular pacing. Whilst some aspects of left ventricular remodelling can be assessed, the entire dataset must be interpreted with the proviso that the patient is being imaged while in a non-routine rhythm that may negatively impact contractile function and valvular regurgitation [8]. Ideally, any assessment of cardiac function should take place with CRT enabled. In this review we consider the role of CMR prior to implantation and how it could be utilised following CRT implantation.

CMR prior to CRT Implantation

Indication

Late gadolinium enhancement (LGE) imaging, unique to CMR is able to identify scar, adding further diagnostic and prognostic information [9] and since the severity of scarring predicts the remodelling response[10], may also have a role in identifying those most likely to respond. Specifically, a large volume of scar (>33%) and transmurality (>51%) are predictors of a poor response to CRT [11]. A larger scar mass and percentage is also associated with a greater incidence of appropriate implantable cardioverter defibrillator (ICD) therapy [12] which might be relevant in future pre-implant discussions regarding the need for CRT with a defibrillator (CRT-D) or without (CRT-P). Furthermore, mid-wall fibrosis in non-ischaemic cardiomyopathy patients receiving CRT, predicts a poorer prognosis, closer to that of those with an ischaemic aetiology [13].

Response and left ventricular lead placement

Whilst CMR can be used for visualisation of the coronary vein for LV lead implantation it is arguably more valuable in identifying areas that should be avoided [14, 15]. Combining scar data with non-contact endocardial mapping to identify areas of slow conduction allows for an optimisation of haemodynamic response,[16] whilst combining scar data with regional contractility data can also predict long-term remodelling response more effectively than standard echocardiography [17]. A large study (n=559) conducted by Levya et al [18] combining coronary angiography with CMR imaging (figure 1) described that avoiding scar improved response to CRT, resulting in fewer hospitalisations and death.

Hence, it seems that CMR is a valuable tool to optimise CRT lead position. Importantly, these studies were predominantly carried out before the advent of MR conditional CRT devices such that none used CMR to assess outcomes.

Imaging following CRT implant

Current methods of imaging with CRT active for optimisation and response

CRT leads to a more coordinated contraction of both ventricles, and implantation is associated with acute haemodynamic improvements [19] as manifested by reduced mean pulmonary capillary wedge pressure, systolic pulmonary artery pressure and left ventricular end-diastolic pressure one month after implantation [2], and improvements in left ventricular structure and function [23].

There are limited data confirming the clinical benefits of post-implant CRT optimisation of atrio-ventricular and ventricular-ventricular timing. Contractility via invasive dP/dt_{max} is accurate and reproducible but inconvenient and invasive, making

it often only practical at the time of implantation [20, 21]. Therefore, non-invasive echocardiographic optimisation has become routine. However, the variability in chamber volume estimation is too great to be clinically useful and timing optimisation therefore focuses on the timings of valvular flows, contraction measured by tissue Doppler imaging, or strain imaging each of which are of limited clinical value, are time consuming and relate poorly to haemodynamic variables [22-24].

Ventricular reverse modelling is a key marker of response to CRT. There is a reliable and close association between improved ventricular structure and function, usually assessed by echocardiography following drug or device intervention and the benefits of that treatment on mortality [25, 26].

Current and potential roles of CMR following CRT implantation

It is possible to scan patients with CRT devices whilst the MR safe mode is activated, however the compliant mode is typically RV pacing rather than biventricular pacing. There are two issues with this: firstly, scans will not be representative of normal CRT function in the patient. Moreover, RV pacing is associated with worse haemodynamics, worse mitral regurgitation, autonomic dysfunction, regional blood flow abnormalities and the dyssynchrony can lead to difficulties with volume and dimension analysis [1, 27].

Hence, in order to achieve a comprehensive and reliable assessment of heart function in the patient's usual state, the long-term goal must be to image with biventricular pacing activated. This has a series of potential benefits that are not currently possible:

1) Optimisation – Left ventricular volumes and cardiac output (using cine and/or phase contrast imaging) could be quantified for various CRT settings to identify optimal settings for individual patients.
2) Assessment of non-response – Bertini et al [28] have shown that CMR is a valuable tool for identifying appropriate lead placement. Approximately one third of patients do not respond to CRT in terms of symptoms or reverse remodelling [29]. With biventricular pacing active it would be possible to assess true ventricular wall movement of people who have responded poorly or not at all to CRT.
3) Monitoring – Ventricular function is likely to change following CRT implantation. This will largely be through a combination of remodelling and reverse remodelling. By directly visualising cardiac volume and movement it would be easier to identify any significant change in functionality and enables the possibility of further optimisation.
4) An extremely valuable tool for research – Due to its high versatility and low inter-study variability, CMR is a powerful platform. A single scan gives significant data and can be virtually re-run to obtain desired outputs giving increased value [30]. A number of key areas could be investigated further:
    a. As the gold standard in assessing the RV, it would be useful to monitor changes in function with CRT active. RV remodelling may differ to the LV and also correlate with other parameters such as quality of life.
    b. Upgrading from RV to CRT pacing suggests improved perfusion and function using single photon emission computed tomography [31]. CMR could more accurately assess the improvements without exposure to radiation. With the use of late gadolinium areas of

ischaemia could be easily identified and potentially acted on via percutaneous intervention.

c. Analysing blood flow – Aortic and pulmonary flow can be accurately visualised using phase contrast or 4d flow techniques to quantify haemodynamic response to CRT [32].
d. Quantifying and predicting beneficial and adverse left ventricular remodelling – CMR is superior to most other techniques in measuring LV volumes [33], thus it could be utilised to predict and accurately track this disease process [34].

Therefore, as the most reliable and reproducible method of determining changes in LV structure and function, CMR has a high potential to become an integral part of the follow-up program for patients with CRT assessing both response and the effects of optimisation. The limiting factors are accessibility, patient acceptability and being more cumbersome than other technologies such as echocardiography. In general, a CMR scan takes longer to complete than an echocardiogram at around 45 minutes. This depends largely on the scanning sequence used, the base heart rate of the patient (a faster heart rate giving slightly faster scans), the specific question being asked and patient compliance. Thus, in the future CMR might initially develop into a test undertaken in patients with a suboptimal response to CRT.

Important procedural aspects of CMR after CRT implantation

Safety: Potential risks of CMR to a pacemaker patient

Prior to the advent of MR conditional devices there were concerns that pacemaker devices being exposed to high strength magnetic fields and radiofrequency pulses

could lead to transient or permanent damage to the battery, circuitry, leads or the heart itself [35, 36]. It became apparent that the multiple electromagnetic fields can create vibration and heating within the generator and leads through the induction of current. This in turn can give inappropriate sensing of the leads causing a failure to pace or a device malfunction including a reset. Reluctance from physicians to commit patients to a MR scan formed, potentially impacting on patient care [37].

The concerns led to industry redeveloping devices and programming options to improve MR tolerance. Devices have minimised their ferromagnetic content and gained solid state technology. Furthermore, filters are used reducing transmission of certain frequencies within the device and leads thus limiting detrimental energy transfer with software complementing “MR safe mode” [38]. The proprietary MR safe mode can only be initiated after a rigorous device integrity check. Once initiated it locks out settings that would otherwise cause interference and susceptibility with magnetic field exposure. Despite the ability to scan patients with a number of therapies are active, there are no known studies investigating this area using CMR.

There are also issues with the rate of energy transfer to healthy tissue via MR. The specific absorption rate is often unremarkable in the majority of cardiac scans; however it can accumulate with certain pulse sequences such as 4D flow and stronger magnetic field strengths such as 3.0T or above. Importantly, safety limits are built into scanning software with warnings and automatic cut-off when beyond reasonable thresholds. Fortunately issues around high specific absorption rate exposure are transient with few recorded significant events and no known associated long term effects [39].

Following a series of studies finding minimal interaction with MR and cardiac devices, the European Society of Cardiology deemed in 2008 that patients with implanted devices could undergo a magnetic resonance imaging scan if appropriate safety considerations were made [40]. Large scale studies have shown that neither non-cardiac nor cardiac scans are associated with death, device or lead failure in this context (table 1). Furthermore, complications are temporary and only in the rarest of incidents have resulted in subsequent intervention required; such cases are often related to violations of modern scanning safety protocol.

Pre-scan device checks

Most modern implanted CRT devices are labelled as MR conditional resulting in a relatively standard protocol across hospitals. Prior to each MR scan, cardiac or otherwise, a routine device check is conducted. This is primarily to establish a baseline set of parameters including lead sensing, voltage threshold and lead impendence. Each major manufacturer has a MR safe mode that vary slightly (table 2), derived from pre-clinical and clinical testing, though typically involve either AOO or DOO pacing with high outputs. Most manufacturers (except Biotronik and Boston Scientific) disable CRT; furthermore if bradycardia pacing is required it is achieved with high output RV VOO pacing. It is advised that a device check is conducted before changing device settings to an MR compatible mode.

Monitoring

When altering pacemaker settings it is crucial to confirm the resultant rhythm is not detrimental to the patient; a cardiac monitor should be in place throughout the scan

with regular patient contact. Notably, some changes such as varying voltage can be uncomfortable to the patient by causing phenomenon such as muscle twitching and diaphragmatic stimulation via high output RV pacing. Once the scan is complete, the device is reverted to pre-scan settings and followed up with a repeated device check focusing on the leads and battery. This ensures that neither the patient or device have been negatively affected during the scan nor are at future risk.

Image quality optimisation

In the presence of an implanted cardiac device, cardiac scanning is particularly associated with artefacts that can make the images more difficult to interpret [41] (figure 2).

Most relevant for implanted devices are susceptibility artefacts. These are created by the difference in magnetic properties of distinct tissue and materials. This interaction causes protons to become dephased giving bizarre patterns on the image [42]. Metallic objects or those interfacing with air often cause distortions manifesting as areas of increased or absent signal. Pacemakers cause susceptibility artefacts primarily from the generator rather than the leads (due to increased metal content), an issue exacerbated at higher magnetic field strengths.

In order to counter these, particular scanning protocols are employed. Currently, the most common technique for cine imaging in patients without a cardiac device is steady-state free precession (SSFP.) Prior to the development of SSFP, gradient echo (GRE) was widely used. It was superseded due to reduced tissue contrast and requiring longer breath-hold. In device patients, GRE has been shown to produce

fewer artefacts and non-diagnostic images than balanced SSFP with image quality significantly better for both the left and right ventricle [43]. Thus, in patients with cardiac devices and suboptimal balanced SSFP imaging, GRE is a useful option. Scanning techniques are developing at a rapid rate; notably the recent study by Hilbert et al [44] has confirmed the utility of alternative protocols to help produce diagnostic grade images.

LGE imaging can be used with both SSFP and GRE for tissue characterisation to delineate areas of scar. Conventional LGE imaging is vulnerable to hyperintensity artefacts particularly from the generator which appears bright on the image. This artefact can either be inappropriately misdiagnosed as scar or impair imaging to the extent that it is non-diagnostic. This problem can be overcome by the use of wideband LGE in which the myocardial nulling caused by the device artefact can be overcome by using a wider band inversion pulse [45]. Since patterns of interference are not consistent it is likely that tailored scan settings for manufacturers and device types will be developed to reduce artefacts [46]. Importantly, whilst LGE does not require any further equipment or processing time, it is associated with increased specific absorption rate by approximately 20% when compared with routine scans [47].

The need for GRE increases the duration of the scan and may prolong breath holding which is a particular problem for patients with CHF. Future technical advances to reduce acquisition time and breath-holding will be particularly beneficial in this patient group. Renal impairment is also a concern and often co-existent with heart failure, potentially prohibiting the use of gadolinium based contrast agents.

Potential process of CMR scanning with CRT on

There are challenges in scanning a patient with CRT active which can largely be overcome with recent advances in both device and CMR technology. We propose a protocol for patients with implanted CRT devices to streamline scanning (figure 3) which limits artefacts, maintains de facto CMR image standards and ensures patient safety and comfort.

Patient safety is paramount and maintained by deviating minimally from current CMR procedure and a high level of due diligence with regards to device review. Artefact limitation can be achieved with relatively simple measures. Appropriate positioning of the patient in the scanner and careful skin preparation to avoid incorrect ECG triggering help obtain high quality images. A GRE scan can be used to obtain images quickly and mitigate artefacts from devices in situ. Experienced radiographers and cardiac physiologists must be involved to reduce artefacts and maximise safety. Ideally, a CMR imaging expert should also be present to facilitate live adjustment of the imaging process to ensure that the images obtained are of the highest quality and subsequently enable a robust analysis. If CRT optimisation is required, the scan can be repeated altering variables such as A-V and V-V delay. With improvements in wireless communication particularly Bluetooth technology, it is feasible that CRT programming could be changed whilst the patient remains in the scanner. This approach would allow left ventricular volumes and cardiac output (using cine and/or phase contrast imaging) to be easily quantified for each CRT setting, identifying optimal settings for each patient.

It is important that in a time of rapidly improving technologies, persistent efforts are made to maximise on the potential outcomes for patients. We look forward to pilot and randomised studies investigating the utility of CMR in this cohort. Scanning patients with CRT active is likely not only viable but an important step in optimising therapy and the responder rate. Indeed the sheer utility of CMR may represent a model shift in care for patients post implantation.

Conclusions

CMR offers significant utility in patients with heart failure; furthermore, advances in CMR and CRT technology mean that scanning with CRT active is feasible. To achieve this routinely in both a clinical and research setting, a multidisciplinary working approach is required with cardiac physiologists, MR radiographers, imaging experts and clinicians. This could lead to significant benefits including device optimisation, improved patient selection, prognostication and understanding mechanisms of non-response.

Conflicts of interest

Dr. Koshy is a PhD fellow on a PhD program sponsored jointly through an unconditional research grant from Medtronic UK and the University of Leeds.

Dr. Witte has received unconditional research funding from Medtronic; has served as an advisor for Medtronic and at the time of manuscript preparation held an NIHR-Clinician Scientist award.

Dr Gierula holds an NIHR post doctoral fellowship.

Dr Swoboda has no conflicts to declare.

Figures

Figure 1 – Adapted from Levya et al [18] with permissions kindly received from BioMed Central. Mapping LV lead positions. The longitudinal distance from the atrioventricular plane to the lead tip, in a base-to-apex direction, is quantified using the 30° right anterior oblique fluoroscopic view (A). This longitudinal distance is transposed to the four-chamber CMR view (B), so as to determine the LGE-CMR short axis slice (yellow line, C) that corresponds to the LV lead tip position. The 30° left anterior oblique fluoroscopic view (D) is then used to determine the circumferential position (yellow arrow). The longitudinal and circumferential coordinates permit localization of the LV lead tip in relation to myocardial segments and myocardial scars, which appear as white enhancement on LGE-CMR (white arrow).

Figure 2 – Imaging strategies to decrease the artefact in patients. Steady state free precession imaging is commonly used but is associated with artefacts in patients with CRT-D (A). The artefact can be reduced by using a gradient echo sequence, albeit at the cost of a longer breath-hold and less contrast between myocardium and blood pool (B). Conventional late gadolinium enhancement imaging is impaired by severe artefact making identification of the apical myocardial infarction difficult (C). The imaging is improved by use of a wideband late gadolinium enhancement sequence, where the apical myocardial infarction can be clearly seen, marked as a red asterix (D).

Figure 3– Flow chart of the potential approach to scanning patients with CRT devices and biventricular pacing active including CMR. (A) Still images of the planning survey with artefact (white asterisk) from the device generator, (B) cine scan with LV and RV lead artefacts (blue and red asterisks respectively), (C) ischaemia testing with perfusion defect indicating septal wall infarct (red arrow) and (D) scar assessment also identifying lateral wall infarct (blue arrow).

Tables

Table 1 – Large trials (n>100) of MRI scanning in patients with implanted cardiac devices

Author	Year of publication	Number of patients scanned	Device type	MRI conditional	MRI Field strength (Tesla)	MRI scanning protocol	Significant complications
Hilbert et al [44]	2018	128	CRT, ICD & PM	Mixture	1.5	Cardiac	None (No changes to device performance or adverse events were observed)
Lupo et al [48]	2018	120	ICD & PM	No	1.5	Routine including cardiac	No adverse events were observed. One temporary communication failure was observed (0.08%).
Nazarian et al [49]	2017	1509	ICD & PM	No	1.5	Routine including cardiac	In 9 examinations (0.4%) the device reverted to a transient back-up programming mode without long-term effects.
Ching et al [50]	2017	140	PM	Yes	1.5	Cardiac	None
Mason et al [51]	2017	178	ICD & PM	Mixture (82% non-conditional)	1.5	Routine including cardiac	None
Russo et al [52]	2017	1246	ICD & PM	No	1.5	Routine excluding thoracic	One patient required generator replacement following scanning whilst in unsafe device settings. In 6 examinations (0.04%) the device reverted to a transient back-up programming mode without long-term effects.
Schwitter et al [53]	2016	156	ICD	Yes	1.5	Cardiac	None
Higgins et al [54]	2016	398	ICD & PM	No	1.5	Routine including cardiac	None
Bailey et al [55]	2016	221	PM	Yes	1.5	Cardiac & Thoracic spine	One adverse event (0.4%) possibly related to the implanted system and scan.
Awad et al [56]	2015	153	ICD	Yes	1.5	Cardiac & Thoracic	None

						spine	
Shenthar et al [57]	2015	177	PM	Yes	1.5	Routine including cardiac	None
Friedma n et al [58]	2013	171	PM	Mixture	1.5	Routine including cardiac	None
Schwitter et al [59]	2013	150	PM	Yes	1.5	Cardiac	None
Gimbel et al [60]	2013	177	PM	Yes	1.5	Chest and head	None
Nazarian et al [61]	2011	438	ICD & PM	No	1.5	Routine including cardiac	In 3 patients (0.007%) the device reverted to a transient back-up programming mode without long-term effects
Wilkoff et al [62]	2011	258	PM	Yes	1.5	Head and lumbar spine	None
Strach et al [63]	2010	114	PM	No	0.2	Routine excluding cardiac	None
Mollerus et al [64]	2010	103	ICD & PM	No	1.5	Routine including cardiac	One pacemaker reverted to transient back-up programming requiring reprogramming

CRT – Cardiac resynchronisation therapy, ICD - Implantable cardioverter defibrillator, MRI – Magnetic resonance imaging, PM – Pacemaker (conventional and dual chamber pacemakers).

Table 2– Comparing default MR compatible settings between major CRT manufacturers.

Parameter	Abott (Previously St. Jude Medical) settings	Biotronik settings	Boston Scientific settings	Medtronic settings
Lead paced	RV	BiV or RV	BiV or RV	RV
Tachycardia therapy disabled?	Yes	Yes	Yes	Yes
CRT disabled?	Yes	Yes	No	Yes
HR range	30-120	70-160	30-110	30-120
Increase output?	Yes, increased to 5V with 1ms as support lead (de facto)	Yes	Yes	Yes
Fixed pacing mode (non-sensing)	Yes (Reverts to VOO, AOO, DOO)	Yes	Yes	Yes

BiV – Biventricular, RV – Right ventricle,

Supplementary material

Comparing SSFP and GRE 4 chamber MRI views.mp4

Video 1 – Cine CMR in a 49 year old female with CRT active at 90bpm (DOO) over 1 second, showing improved image acquisition can be improved from steady state free-precession (SSFP) on the left with a gradient echo (GRE) sequence on the right. This produces significantly less artefact.

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