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Uses and potential for cardiac magnetic resonance imaging in patients with cardiac resynchronisation pacemakers

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Conflicts of interest

Dr. Koshy is conducting a fellowship with an unconditional research funding provided by Medtronic to the University of Leeds.

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Abstract

Cardiovascular magnetic resonance (CMR) imaging has been shown to be safe as an imaging modality for patients with cardiac resynchronisation (CRT) pacemakers. As the gold standard for measuring cardiac volumes, mass and ejection fraction, CMR has underutilised potential in improving diagnostics and care for patients implanted with CRT devices. A number of studies have already highlighted a role in optimising left ventricular lead placement. There is also significant evidence the scanning is useful prior to implantation to predict outcome and optimise device effect through lead placement. By employing modern technology and techniques, there is scope to improve CMR utility post implantation by potentially scanning in higher field strengths and whilst CRT is active. These advances are expected to translate to an improved responder rate and patient outcomes.

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

Background

CRT and CMR

Heart failure is a common condition affecting 1-2% of the adult population in developed countries, increasing to above 10% in those aged over 70 years [1]. Shortness of breath and reduced exercise capacity are often are the initial presenting complaints with further imaging required such as echocardiography to make the initial diagnosis. Cardiovascular magnetic resonance (CMR) is considered the gold standard for investigating the aetiology of heart failure due its ability to identify ischaemia and ventricular dimensions. It has further utility in the diagnosis of uncommon conditions including sarcoidosis and haemochromatosis [1]. High quality tissue characterisation and low inter-observer variability allows CMR act as a single imaging tool for both diagnosis and prognostication [2].

Cardiac resynchronisation therapy (CRT) pacemakers are routinely implanted in patients with reduced ejection fraction heart failure and an associated conduction issue such as left bundle branch block (LBBB) [1]. Dyssynchrony is over-represented in the heart failure population (approximately 25%) and increases the 1 year mortality risk by 70% [3]. CRT devices cause pre-excitation within the left and right ventricles through leads placed at the right atrium, right ventricle and coronary sinus (left ventricle). This helps co-ordinate contraction precisely resulting in improved stroke volume and myocardial efficiency [4]. Following implantation, patients generally have an increased exercise capacity with fewer symptoms, improved haemodynamics and reduced mortality [1, 5, 6]. CRT devices can also have a defibrillator fitted (CRT-D) conferring additional survival in selected populations such as patients with diabetes or an ischaemic aetiology [7].

There has been a longstanding caution in applying CMR techniques in patients with a CRT device due to isolated reports of damage to pacemaker devices, ranging from issues around the generator, circuitry or the leads which in turn could damage myocardium [8, 9]. However, retrospective observational studies in patients with pacemakers scanned incidentally have suggested that the rate of complications, even with standard non-MRI-conditional devices is incredibly rare. The European Society of Cardiology issued guidance in 2008 that patients could be eligible for CMR if reasonable considerations were made both in selection and the scanning techniques employed [10]. More recent registry and off-label studies have confirmed the relative safety of CMR if precautions are taken [11, 12]. Furthermore, pacemakers appear to be safe in a standard MRI scanner without monitoring taking place [13]. However, to improve confidence, over the past few decades device compatibility with magnetic resonance has garnered interest. Industry have made significant strides in reducing ferromagnetic content within the devices in addition to filters to block out certain magnetic frequencies and software to optimise settings to reduce the impact of exposure. This has led to the present situation where the majority of pacemakers and CRT devices routinely implanted are MRI conditional. Similarly, CMR has improved in image quality, scanning time and accessibility to patients. Currently it is used as part of a multimodality-imaging package in this cohort of patients, showing utility pre-implantation in optimising the lead placement and the response rate [14, 15].

In this report we will explore the current uses of CMR in patients with a CRT device implanted and speculate on the future application of this scanning technique. We believe that CMR is likely to become the most useful imaging modality for heart failure patients not only considered for implantation but also for monitoring response subsequently.

Current applications of CMR

MRI uses a combination of strong magnetic fields and radiowaves to create images. A magnetic moment is generated within the hydrogen nuclei causing alignment generally in the direction of the static external magnetic field. This also creates additional spin (precession) around the hydrogen ion. When the radiofrequency pulse matches the product of internal frequency of the ion and magnetic field strength, resonance is achieved which forms the image [16]. The combination of repeated electromagnetic pulses in the presence of a constant strong magnetic field is the driver of potential damage to a pacemaker. Whilst improvements to the CRT hardware and software have made CMR viable following implantation, patients with a CRT-D remain with a higher risk of arrhythmias such as ventricular fibrillation or tachycardia due to increased structural disease. Furthermore, patients with CRT-Ds have greater propensity to short-circuit whilst the images are more degraded due to large areas of artefact [17]. Often, alternative MRI scan protocols are carried out to obtain a diagnostic grade image [18]. All of these issues in conjunction with strict programmable settings and scanning techniques limit the current uses of CMR in patients with a CRT device. This is complicated further by the "MRI safe mode," a requirement for the use of CRT devices in a MRI scanner. The mode generally switches off therapies, fixes a minimum heart rate and has right ventricular pacing active.

Despite these limitations, if appropriate precautions are taken, CMR is viable in patients with a CRT device for a broad set of indications:

1. Assessment of aetiology of heart failure – For a selection of patients it remains helpful to investigate the cause of left ventricular systolic dysfunction
2. Assessment of ischaemia or fibrosis - Late gadolinium enhancement is utilised to evaluate fibrosis and scar formation. This technique has been validated against histopathology [19] and creates a large contrast between normal and scarred tissue. The distribution pattern of these tissue types can be analysed to distinguish between ischaemic and non-ischaemic pathologies.
3. Assessment of ventricular parameters, specifically; volume, mass and ejection fraction.
4. Investigating wall motion - The myocardial tissue usually moves in three planes: radially, longitudinally and circumferentially. With therapies active it would be expected that wall motion would return to a more normalised movement enabling the relatively small organ to generate a large amount of force. Conventional MRI gives a high quality image of the heart with the ability to analyse motion and the displacement of the inner and outer wall. This technique allows measurement of radial strain to be made relatively accurately in a routine scan. Importantly, radial strain is generally the largest strain subtype and associated with

wall thickening [20]. The other types of strain assessment require advanced imaging techniques. Wall motion patterns with an appropriately placed left ventricular lead have been independently linked to CRT response [21].

Despite these advances, CMR remains underutilised in patients with a CRT device. Many hospital in the UK do not offer a CMR service to patients with a cardiac device in situ [22]. This is largely related to perceived concerns around scanning this cohort, logistical issues and a lack of support. The hospitals that do use CMR for implanted cardiac devices generally conduct fewer than 10 scans per year. Further research and communication is needed to bridge this gap between feasibility and practical improvements in care.

Potential issues around CMR scanning

Standard MRI in the UK is conducted in scanners with a field strength of 1.5 Tesla. Advances in imaging technology has led to many institutions owning 3T or 7T scanners that are largely used for research, though there is increasing overlap with clinical practice. Increasing the field strength of the scanner has some obvious benefits including improved signal to noise ratio, spatial resolution and potentially faster scanning [23]. However the trade-off is an increased rate of artefacts and likelihood of reaching the specific absorption rate (SAR) limit for patients. Artefacts (routinely caused by implanted cardiac devices) are particularly exacerbated by the higher field strength often manifesting as large areas of void within the image. Modern pacemakers allow for a SAR limit of 2W/Kg for whole body scanning. The SAR applied on a patient relates to the frequency, intensity and scanning protocol used. Higher SAR will cause greater physiological stress (such as heating) to cells though could enable faster scanning. However, there are few recorded events of short or long term patient harm from passing these limits [16]. Modern scanning techniques means that SAR levels are kept to a minimum with restrictions built in to the software to cut off scanning when beyond patient derived limits.

This is also an issue in scanning patients with conditions including heart failure who often have irregular or difficult to control breathing. Routine imaging relies on respiratory triggering combined on cardiac gating and arrhythmia rejection [24]. There is currently significant validation work on-going to dramatically reduce the need for breath holding by using free breathing scan techniques. Advances in free breathing protocols are likely to result in faster scan times with arguably less image variance.

The current protocol of scanning patients in “MRI safe mode” via RV pacing is safe but contentious. The CMR image may not be truly representative of normal cardiac function for the patient, i.e. with CRT therapies active. It is hoped that in the future pilot studies likely in collaboration with industry will scan in patients with biventricular pacing. This step may well provide the foundation for both device optimisation and prediction of treatment response. Late gadolinium enhancement could also be used in this cohort to predict outcomes as already evidenced in patients with dilated cardiomyopathy [25]. Furthermore, recent study has suggested that non-conditional devices rarely present a danger to the patient nor become obviously damaged when exposed to routine scans at different locations of the body including the thorax [26]. As MRI conditional devices are generally more expensive and sometimes less structurally ideal, increasing confidence around older non-CMR conditional devices means that CMR could therefore be accessible to more patients. The gains are potentially increased further when considering that replacing older non-conditional leads to produce a full “MRI system” increases the adverse event risk from 4% to 15% [27].

Summary

CMR is a safe, under-utilised, high value imaging choice for patients with a CRT device; enabling gold standard assessment of aetiology, ventricular volume, mass and ejection fraction. Advances in both scanning techniques and device technology are expected to lead to improvements in accessibility, device optimisation and patient outcomes.

Expert commentary

Indications for CRT implantation vary significantly around the globe [28]. CMR could be positioned as a single solution in the patient journey from the diagnosis of heart failure to assessment of response to CRT [29]. Novel parameters such as scar burden, myocardial viability and mechanical dyssynchrony would also be possible from a reduced number of imaging procedures. Advanced MRI techniques including magnetisation tagging, tissue phase mapping strain encoded imaging allow for dense assessment of motion throughout the cardiac walls [20]. These techniques allow longitudinal and circumferential strain to be analysed. This would be fascinating, giving us a more accurate picture of the complex movement of the heart in this cohort of patients. Echocardiographic assessment have already eluded to an improvement in all three types of myocardial contraction with CRT therapies active[30].

CMR also shows great promise in imaging the right heart which is poorly imaged by other techniques; right ventricular function is increasingly relevant in patients with left ventricular systolic dysfunction [31]. Right ventricular dimensions can be obtained accurately with work in progress to apply techniques including mapping to analyse wall motion accurately [20].

As CMR becomes standardised post CRT implantation, it is expected that cardiac images and profiles are created for each patient. Advanced predictive modelling would show the expected outcome not only with CRT therapies active but also with other device parameters. Ideal device settings could be generated which may evolve with the patient's response or disease process. It may become feasible to accurately predict degradation in ventricular function and hospitalisation as evidenced in patients with ICDs [32].

Key Issues

The utilisation of CMR whilst CRT is active will enable direct visualisation with gold standard assessment of the cardiac augmentation with CRT active. This will answer a number of questions currently unclear in the treatment of heart failure patients including:

- How is ventricular contraction improved following CRT and over what time course are these improvements expected?
- Can CRT therapy be optimised further by altering the settings of the pacemaker and re-evaluating changes with CMR?
- How does right ventricular function change with CRT and is this important?
- Does the aetiology of heart failure play a significant role in cardiac function with CRT and does it alter outcomes?

<u>5 Year plan</u>

Indications for CMR in the context of device therapy will become common, both before and after implantation. By enabling CRT to be active during assessment it becomes possible to identify responders at an earlier stage and also generate outcome profiles based on the pre and post implantation assessment. CMR itself will represent a single solution for most of the workup of patients requiring CRT, improving candidate selection, lead placement and even treatment response assessment. With advances in technology it will be possible to alter device settings wirelessly, enabling easier optimisation and assessment whilst the patient undergoes scanning.

References

1. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail. 2016;18(8):891-975.
2. Swoboda PP, Plein S. Established and emerging cardiovascular magnetic resonance techniques for prognostication and guiding therapy in heart failure. Expert Rev Cardiovasc Ther. 2014;12(1):45-55.
3. Baldasseroni S, Opasich C, Gorini M, Lucci D, Marchionni N, Marini M, et al. Left bundle-branch block is associated with increased 1-year sudden and total mortality rate in 5517 outpatients with congestive heart failure: a report from the Italian network on congestive heart failure. Am Heart J. 2002;143(3):398-405.
4. Sundell J, Engblom E, Koistinen J, Ylitalo A, Naum A, Stolen KQ, et al. The effects of cardiac resynchronization therapy on left ventricular function, myocardial energetics, and metabolic reserve in patients with dilated cardiomyopathy and heart failure. J Am Coll Cardiol. 2004;43(6):1027-33.
5. Leclercq C, Cazeau S, Le Breton H, Ritter P, Mabo P, Gras D, et al. Acute hemodynamic effects of biventricular DDD pacing in patients with end-stage heart failure. J Am Coll Cardiol. 1998;32(7):1825-31.
6. Inage T, Yoshida T, Hiraki T, Ohe M, Takeuchi T, Nagamoto Y, et al. Chronic cardiac resynchronization therapy reverses cardiac remodelling and improves invasive haemodynamics of patients with severe heart failure on optimal medical treatment. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2008;10(3):379-83.
7. Morani G, Gasparini M, Zanon F, Casali E, Spotti A, Reggiani A, et al. Cardiac resynchronization therapy-defibrillator improves long-term survival compared with cardiac resynchronization therapy-pacemaker in patients with a class IA indication for cardiac resynchronization therapy: data from the Contak Italian Registry. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2013;15(9):1273-9.
8. Erlebacher JA, Cahill PT, Pannizzo F, Knowles RJ. Effect of magnetic resonance imaging on DDD pacemakers. Am J Cardiol. 1986;57(6):437-40.
9. Langman DA, Goldberg IB, Finn JP, Ennis DB. Pacemaker lead tip heating in abandoned and pacemaker-attached leads at 1.5 Tesla MRI. J Magn Reson Imaging. 2011;33(2):426-31.
10. Roguin A, Schwitter J, Vahlhaus C, Lombardi M, Brugada J, Vardas P, et al. Magnetic resonance imaging in individuals with cardiovascular implantable electronic devices. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2008;10(3):336-46.
11. Russo RJ, Costa HS, Silva PD, Anderson JL, Arshad A, Biederman RWW, et al. Assessing the Risks Associated with MRI in Patients with a Pacemaker or Defibrillator. New England Journal of Medicine. 2017;376(8):755-64.
12. Strom JB, Whelan JB, Shen C, Zheng SQ, Mortele KJ, Kramer DB. Safety and utility of magnetic resonance imaging in patients with cardiac implantable electronic devices. Heart rhythm. 2017;14(8):1138-44.
13. Bertelsen L, Petersen HH, Philbert BT, Svendsen JH, Thomsen C, Vejlstrup N. Safety of magnetic resonance scanning without monitoring of patients with pacemakers. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing,

arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2017;19(5):818-23.
14. Bertini M, Mele D, Malagu M, Fiorencis A, Toselli T, Casadei F, et al. Cardiac resynchronization therapy guided by multimodality cardiac imaging. Eur J Heart Fail. 2016;18(11):1375-82.
15. Behar JM, Claridge S, Jackson T, Sieniewicz B, Porter B, Webb J, et al. The role of multi modality imaging in selecting patients and guiding lead placement for the delivery of cardiac resynchronization therapy. Expert review of cardiovascular therapy. 2017;15(2):93-107.
16. Westbrook C, Roth C, Talbot J. MRI in practice. 4th ed: Wiley-Blackwell; 2011.
17. Sommer T, Bauer W, Fischbach K, Kolb C, Luechinger R, Wiegand U, et al. MR Imaging in Patients with Cardiac Pacemakers and Implantable Cardioverter Defibrillators. RoFo : Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin. 2017;189(3):204-17.
18. Schwitter J, Gold MR, Al Fagih A, Lee S, Peterson M, Ciuffo A, et al. Image Quality of Cardiac Magnetic Resonance Imaging in Patients With an Implantable Cardioverter Defibrillator System Designed for the Magnetic Resonance Imaging Environment. Circulation Cardiovascular imaging. 2016;9(5).
19. Kim RJ, Fieno DS, Parrish TB, Harris K, Chen EL, Simonetti O, et al. Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. Circulation. 1999;100(19):1992-2002.
20. Chitiboi T, Axel L. Magnetic resonance imaging of myocardial strain: A review of current approaches. Journal of magnetic resonance imaging : JMRI. 2017;46(5):1263-80.
21. Hartlage GR, Suever JD, Clement-Guinaudeau S, Strickland PT, Ghasemzadeh N, Magrath RP, 3rd, et al. Prediction of response to cardiac resynchronization therapy using left ventricular pacing lead position and cardiovascular magnetic resonance derived wall motion patterns: a prospective cohort study. J Cardiovasc Magn Reson. 2015;17:57.
22. Sabzevari K, Oldman J, Herrey AS, Moon JC, Kydd AC, Manisty C. Provision of magnetic resonance imaging for patients with 'MR-conditional' cardiac implantable electronic devices: an unmet clinical need. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2017;19(3):425-31.
23. Kuhl CK, Traber F, Schild HH. Whole-body high-field-strength (3.0-T) MR Imaging in Clinical Practice. Part I. Technical considerations and clinical applications. Radiology. 2008;246(3):675-96.
24. Krishnamurthy R, Pednekar A, Atweh LA, Vogelius E, Chu ZD, Zhang W, et al. Clinical validation of free breathing respiratory triggered retrospectively cardiac gated cine balanced steady-state free precession cardiovascular magnetic resonance in sedated children. Journal of Cardiovascular Magnetic Resonance. 2015;17(1):1.
25. Chimura M, Onishi T, Tsukishiro Y, Sawada T, Kiuchi K, Shimane A, et al. Longitudinal strain combined with delayed-enhancement magnetic resonance improves risk stratification in patients with dilated cardiomyopathy. Heart (British Cardiac Society). 2017;103(9):679-86.
26. Mason S, Osborn JS, Dhar R, Tonkin A, Ethington J-D, Le V, et al. Real world MRI experience with nonconditional and conditional cardiac rhythm devices after MagnaSafe. Journal of Cardiovascular Electrophysiology. 2017;28(12):1468-74.
27. Poole JE, Gleva MJ, Mela T, Chung MK, Uslan DZ, Borge R, et al. Complication rates associated with pacemaker or implantable cardioverter-defibrillator generator replacements and upgrade procedures: results from the REPLACE registry. Circulation. 2010;122(16):1553-61.
28. Bastian D, Ebrahim IO, Chen JY, Chen MC, Huang D, Huang JL, et al. Real-world geographic variations in the use of cardiac implantable electronic devices-The PANORAMA 2 observational cohort study. Pacing and clinical electrophysiology : PACE. 2018.
29. Khidir MJ, Delgado V, Ajmone Marsan N, Bax JJ. Mechanical dyssynchrony in patients with heart failure and reduced ejection fraction: how to measure? Curr Opin Cardiol. 2016;31(5):523-30.

30. Knebel F, Schattke S, Bondke H, Eddicks S, Grohmann A, Baumann G, et al. Circumferential 2D-strain imaging for the prediction of long term response to cardiac resynchronization therapy. Cardiovascular Ultrasound. 2008;6(1):28.
31. Konstam MA, Kiernan MS, Bernstein D, Bozkurt B, Jacob M, Kapur NK, et al. Evaluation and Management of Right-Sided Heart Failure: A Scientific Statement From the American Heart Association. Circulation. 2018;137(20):e578-e622.
32. Zhang Y, Guallar E, Weiss RG, Stillabower M, Gerstenblith G, Tomaselli GF, et al. Associations between scar characteristics by cardiac magnetic resonance and changes in left ventricular ejection fraction in primary prevention defibrillator recipients. Heart Rhythm. 2016;13(8):1661-6.