

Cardiac physiology investigated by new methods of imaging

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Cardiac imaging is the 'bread-and-butter' of cardiology. Current methods include chest X-ray, echocardiography, nuclear scintigraphy, and catheterisation-based invasive techniques. The proliferation of imaging has undoubtedly led to major advances in the specialty. If William Harvey were alive today, however, he might be the first to tell us that the current imaging methods have severe limitations and drawbacks, related to issues such as insufficient resolution and information, the use of radiation, and of invasive procedures associated with risk and discomfort. This article explores the concept that the solution to many of these shortcomings may be the application of cardiac magnetic resonance imaging (MRI).

Compared to the physics of X-rays or of ultrasound, the physics of magnetic resonance (MR) are substantially more complex.¹ In short, atomic nuclei with an uneven number of protons, neutrons or both have the property of a nuclear spin. When these nuclei are exposed to an external magnetic field and are excited by radiofrequency waves they send out a signal in return, termed the free induction decay. These weak radiofrequency signals can be detected by MR coils and used to construct an image. Application of a magnetic field strength gradient allows imaging of the spatial distribution of the nuclear spins. The contrast of an MR image depends on spin density (the number of nuclei susceptible to MR imaging in the tissue), the relaxation parameters T_1 and T_2 , the effects of flow and the type of pulse sequence used. A pulse sequence is a pattern of radiofrequency waves used to excite the nuclear spins.

Anatomy and function

The major advantage of cardiac MR (CMR) is that it is an extremely versatile technique. The ultimate goal for a comprehensive CMR examination would be to obtain, within less than 30 mins of acquisition time and less than 10 mins of post processing time, information on cardiac and great vessel anatomy, cardiac volumes and mass, global and regional contractile function, regional myocardial tissue perfusion, regional tissue characteristics such as viability, inflammation, fibrosis and metabolism, information on the coronary artery lumen, wall and blood flow.

Cardiac MR is now considered the gold standard for

investigation of high resolution cardiac and thoracic anatomy and for measurement of global and regional myocardial function.²⁻⁴ For anatomic imaging, typically turbo-spin echo or half-Fourier acquisition single-shot turbo spin-echo sequences are used, where blood appears dark and myocardium is bright. For imaging of cardiac function, true-FISP (fast imaging with steady-state precession) cine sequences (alternative names: steady state free precession, balanced fast field echo, fast imaging employing steady-state acquisition) are used. Here, chamber blood is bright (bright blood imaging) and myocardium dark. Such images reveal information on global and regional function with unprecedented detail. We are not limited by acoustic windows and can always view the entire heart. The contrast between chamber blood and myocardium is extremely high and allows for accurate determination of the subendocardial border. Right ventricular global and regional function can also be assessed, and, in addition, we are free to select any imaging plane that might yield additional functional information. Typical cine imaging planes include the horizontal long axis (four-chamber view), vertical long axis (two-chamber view), and short axis views. A stack of short axis cine images is obtained, typically using 1 cm slices reaching from the base to the apex of the heart. Each slice is then quantified for myocardial chamber volumes and mass, both in systole and diastole. Slice volumes are added up to yield extremely reproducible and accurate measurements of myocardial mass, ejection fraction, end-diastolic and end-systolic volumes, both for the left and for the right ventricle. A large number of current clinical heart failure trials have chosen CMR as the imaging modality to monitor changes in left ventricular function and mass.

Perfusion

Cardiac MR allows the assessment of regional myocardial perfusion with unprecedented resolution.⁵ Typically, this is performed as a first pass perfusion study using the MR contrast agent GdDTPA. This contrast agent shortens T_1 relaxation time and thus markedly brightens T_1 -weighted MR images. A bolus of MR contrast is flushed into a peripheral vein, and the passage of the contrast through the

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heart is observed with high spatial and temporal resolution. The contrast first appears in the right ventricle, then passes through the lungs, and then through the left ventricular cavity. Finally, the contrast arrives in the left ventricular tissue, which therefore turns brighter ('enhances'). Areas where contrast arrival is delayed because of an associated coronary stenosis will appear darker on perfusion images, thus allowing the diagnosis of a perfusion deficit to be made. Typically, this is performed before and following vasodilator stress (eg adenosine). Each slice is then divided into segments, and perfusion is evaluated for each segment. This can be achieved qualitatively (eyeballing), semi-quantitatively (perfusion reserve) or using absolute quantification. Three clinical studies (one single centre, two multicentre), each including close to 100 patients, have been published in the past year,⁶ demonstrating a diagnostic accuracy of MR perfusion imaging for the diagnosis of significant coronary artery stenosis in the order of 85–90%. Compared to the traditional approach of imaging myocardial perfusion by nuclear scintigraphy, the MR method has the advantages of much higher spatial resolution including analysis of the transmural extent of perfusion deficits, it is radiation free, much faster (approximately 15 mins) and can be part of a comprehensive CMR exam. Current limitations are the lack of large trials evaluating the prognostic power of perfusion CMR, lack of a uniformly accepted approach to quantification and time-consuming data processing.

Viability

Over recent years, delayed enhancement CMR has been established as the gold standard method for assessment of myocardial viability.⁷ Alternative current methods such as positron emission tomography, nuclear scintigraphy or dobutamine stress echocardiography all have limitations related to resolution, radiation, patient discomfort, availability and requirements for appropriate acoustic windows. Delayed enhancement CMR is performed 10–20 mins after injection of a bolus of GdDTPA, using an inversion recovery sequence. On such

images, acutely necrotic and chronically scarred myocardium appears bright, while normal, stunned and hibernating myocardium is black. This technique allows in vivo infarct imaging in humans with previously unprecedented resolution. Such images yield information on the three-dimensional nature of a myocardial infarction. Planimetry allows accurate quantification of infarct size in per cent of total left ventricular mass, and this information is very useful in clinical practice. Late enhancement CMR is highly superior to single photon emission computed tomography for the detection of subendocardial infarction, which can easily be missed by the substantially lower resolution nuclear technique, but can accurately be depicted with CMR. The clinical relevance of this finding and the prognostic implications of detecting small subendocardial infarcts remain to be determined. Studies have shown that the transmural extent of hyperenhancement strongly predicts the likelihood of improvement of regional myocardial contractility post revascularisation: the large majority of dysfunctional segments without any hyperenhancement improves contractility at six months, while segments with three quarters to full thickness hyperenhancement do not recover.^{8,7}

The advantages of viability imaging by MRI compared to echo or nuclear methods are that:

- delayed enhancement provides by far the highest spatial resolution including analysis of the transmural extent
- it is radiation free
- there is no need to stress the heart
- one contrast agent bolus can serve for analysis of both perfusion and viability imaging.

Angiography

Contrast-enhanced MR angiography is a technique with enormous success in clinical practice, and it can depict almost every vascular territory with superb resolution, with the exception of the coronaries. This technique is in routine use, eg for leg or renal arteriography, or for depiction of the complex anatomy of the large thoracic arteries, for example in aortic coarctation. Another important new application of this technique is pulmonary vein/left atrial angiography, which is of major use to electrophysiologists when performing ablation for atrial flutter/fibrillation.

One area where CMR has not yet fulfilled expectations is MR coronary angiography. Fundamental challenges are that coronary arteries are small structures, which move rapidly with the cardiac cycle and with respiration. Current MR coronary angiography is not a real time technique, data from several cardiac cycles have to be averaged, and echocardiographic triggering and breath-hold or navigator imaging are also required. The current spatial resolution of this technique is limited to just under 1 cubic mm. The largest MR coronary angiography multicentre study⁹ showed a sensitivity for the detection of coronary artery disease of 83%, but only 84% of images were interpretable. Clearly, at the present time, MR coronary angiography is not ready for clinical prime time, and

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substantial further development is needed to achieve this. The great potential of vascular MR for the future, however, lies in the fact that it can go beyond pure luminography, and also yield information on the vessel wall structure, including qualitative and quantitative analysis of atherosclerotic plaque (fibrous cap, lipid core, etc). Furthermore, vessel function can be analysed and flow velocity and arterial distensibility can be determined. It is likely that functional vascular measurements can serve as a more sensitive indicator of early vascular damage than structural images.

Future developments

Finally, there are a number of CMR techniques on the horizon which have not yet made it into clinical practice, but may well do so in coming years. Tagging or tissue phase mapping is used to measure regional myocardial strain. Arterial spin labeling techniques may allow assessment of myocardial perfusion without the use of MR contrast agent. Blood-oxygen-level-dependent imaging allows the assessment of regional myocardial oxygenation. With ^{23}Na -imaging, regional myocardial sodium concentrations can be determined, which are increased in scar tissue. MR spectroscopy opens a window into the non-invasive determination of cardiac metabolism. Higher field magnets (eg 3 tesla) may allow unprecedented resolution. There is also the highly promising field of molecular imaging, which should, in the future, allow myocardial and vascular imaging with molecular specificity.

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