Clinical Applications of Cardiovascular Magnetic Resonance Methods

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Abstract

The application of magnetic resonance to diagnostic medical imaging stands as one of the great scientific achievements in the past 50 years. Magnetic resonance techniques are easily applied to organs which remain stationary during the imaging procedure, such as the brain and musculoskeletal system. Imaging of moving heart structures and circulating blood is considerably more difficult. Clinical application of magnetic resonance to the cardiovascular system remains challenging but continuing technological innovations have enabled cardiovascular specialists to more effectively utilize magnetic resonance in clinical practice as well as for innovative research. Cardiovascular magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) are now being used with increasing frequency for the assessment of patients with cardiovascular disease. This paper will introduce clinicians to the current applications of these flexible and robust tools. A brief introduction will be given to the physics of MRI, the instrumentation and the imaging strategies. The main focus of the article, however, is to review how these techniques are being applied by clinicians in routine daily care.

Keywords: Cardiovascular magnetic resonance methods • Diagnostic medical imaging • Magnetic resonance angiography

Introduction

Terminology can be a stumbling block for clinicians being introduced to the study of magnetic resonance methods. In conventional parlance, the term cardiovascular MRI is used to describe imaging of the heart and blood vessels which is accomplished without using contrast agents. The term cardiovascular magnetic resonance angiography (MRA) is most commonly used when blood vessel imaging is accomplished with the use of intravenous contrast agents. MRA techniques increase the conspicuity of blood vessels and aid in defining vascular pathology (Figure 1).
Basic Principles

Magnetism arises as a result of the motion of charged particles. Many materials exhibit magnetic properties but, in medicine we exploit the hydrogen nucleus to generate images. The hydrogen nucleus, which is abundantly distributed throughout the body primarily in the form of water molecules, both spins and possesses an electric charge. Accordingly, the hydrogen nucleus creates magnetism. When the human body is placed in the external magnetic field of a commercial magnetic resonance instrument a small net magnetic force is produced by the hydrogen nuclei. This net magnetic force can be manipulated and localized in space forming an image which represents the distribution of the aforementioned nuclei. When one looks at a typical magnetic resonance image, one is simply looking at a map of hydrogen nuclei, primarily in the form of water, in the area being interrogated.

A crucial point in magnetic resonance methods is to understand that the magnetic behavior of hydrogen nuclei is highly dependent on the local environment in which they are concentrated. The human body, with its complex latticework of tissues and organs, has a variable distribution and concentration of hydrogen nuclei in solid organs and in the vasculature. Each tissue has 2 unique signatures which describes how the hydrogen nuclei behave in a magnetic field after they have been perturbed by a radiofrequency pulse of appropriate energy. The magnetic behavior within the overall lattice that the nuclei are located is referred to as T1 relaxation (spin-lattice relaxation). The magnetic behavior between adjacent hydrogen nuclei is referred to as T2 relaxation (spin-spin relaxation). T1 and T2 values for typical tissues are well established. The signal produced by hydrogen nuclei and detected by magnetic resonance instruments can be made to be dependent on T1 and T2 characteristics of the area interrogated. With this background, it can now be appreciated that image appearance in MRI is dependent on hydrogen nuclei density, T1 characteristics, T2 characteristics and motion (including blood flow). Although complex, it is just this complexity which can be manipulated by magnetic resonance methods, with and without contrast agents, to provide unparalleled insight into form and function in both normal and pathological states.

Instrumentation

The components of a commercial MR scanner include:
(1) A large superconducting magnet which is always on and provides a continuous and stable field strength.
(2) A series of smaller magnets, referred to as gradient coils, which surround the main magnet. These gradient magnets are switched on and off quite rapidly and transiently create a “gradient” of field strengths in 3 dimensions.
(3) Radiofrequency transmission and receiver coils
A computer to process the information and generate the typical image display. To acquire an image, the patient must lie still in the main bore of the magnet. The local magnetic environment is manipulated through the rapid application of the magnetic “gradients” which, as noted above, surround the main magnet. Radiofrequency energy is applied and absorbed within the imaging area of interest. The combination of gradient application and radiofrequency energy perturbation allows a 3-dimensional signature to be given to the hydrogen nuclei within the imaging plane. The timing chosen for the image field perturbation and the timing chosen for detection are software parameters programmed into the instrument (see Imaging Sequences section below). These techniques facilitate localization and image contrast which result in the generation of medical images capable of exquisite temporal and spatial resolution.

Most MR instruments in clinical use throughout the world operate at field strengths of 0.5 to 1.5 Tesla. For perspective, the earth’s magnetic field is less than 1 Gauss (1 Tesla = 10,000 Gauss). The workhorse instrument for general imaging use is the 1.5 Tesla instrument. Recently, scanners have become commercially available that operate at a field strength of 3 Tesla. For the highest quality CV applications, standard bore configuration magnets are required. It should be noted that scanners are available which do not have a bore configuration (open magnets) but, these instruments are not adequate for most cardiovascular applications. Figure 2 shows the 1.5 Tesla magnet used in our laboratory.

**Imaging Sequences**

There are myriad ways that an MR instrument can be made to interact with tissues of interest. The set of instructions given by the computer to the gradient coils and radiofrequency coils during acquisition is referred to as an imaging sequence. The basic imaging sequences have been designed to highlight a tissue of interest. The blood pool can be made to appear either dark or bright and the acquisition can also be designed to highlight anatomic information or flow information. Spatial resolutions ranging from several millimeters to sub-millimeter can be achieved in any desired plane to highlight anatomy. Very low temporal resolutions can be achieved to highlight function. Cardiac gating is required for cine imaging and in a typical acquisition used to assess ventricular function, cine images with a temporal resolution in the range of 15-30 milliseconds are routinely obtained. Commericially available sequences can provide limited information about tissue characteristics. Further, as will be described later, clinically important information about tissue vascularity and myocardial viability can be obtained following the infusion of MRI contrast agents.

A detailed treatment of imaging sequences is a complex topic which is beyond the scope of this paper but can be found in many standard references. Suffice it to say that imaging sequences are continually being developed by software programmers and many of the new and exciting developments in cardiovascular magnetic resonance methods are being made possible by innovations in this area.

**Contrast Agents**

Agents have been developed which significantly alter the magnetic field behavior of hydrogen nuclei and thereby alter tissue contrast. Most currently available MR contrast agents are chelates of the rare earth metal gadolinium. Gadolinium is not imaged directly, rather the images obtained are a representation of the effect that gadolinium has on adjacent hydrogen nuclei. Gadolinium is effective because hydrogen nuclei in close proximity to gadolinium have a T1 relaxation time that is dramatically lowered when compared to hydrogen nuclei not in proximity to gadolinium. Accordingly, imaging sequences can be chosen to highlight differences in T1 relaxation and these differences can produce excellent tissue contrast. Bolus administration and early imaging, while the gadolinium chelate is still within the vasculature, is used to produce high quality angiograms (MRA). The normally used MR contrast agents diffuse rapidly into the extracellular space and images can be obtained after the infused agent has left the vascular compartment and distributed into the tissues (CE-MRI).

Gadolinium is highly toxic in its elemental state but, gadolinium chelates have been devised with remarkable safety.
profiles. There have been rare but, well described, systemic side effects including anaphylactoid reactions. Serious toxic effects have also recently been reported in patients with renal failure and advanced renal failure should be regarded as a strong relative contraindication to contrast MRI. Despite the small risks associated with their use, gadolinium based agents have been used safely in patients of all ages and contrasted images have greatly improved the diagnostic power of magnetic resonance imaging. The development of improved contrast agents for clinical applications is an area of intense research in laboratories throughout the world.

Safety

A major advantage of MRI is that imaging is performed without exposing the patient to ionizing radiation or iodinated contrast material. Accordingly, as currently applied, MRI is devoid of any known destructive biophysical effects in appropriately selected patients.

There are, however, important safety considerations for MR imaging and many excellent resources are available which deal with safety.

An excellent web based resource is http://www.mrisafety.com/ Standard contraindications include cardiac pacemakers, defibrillators, ferromagnetic intracranial aneurism clips, and various implanted or magnetically activated devices. Most orthopedic hardware can be imaged safely although image degradation is likely to occur if the region of interest is in close proximity to the metallic hardware. Sternal wires, coronary stents, and artificial heart valves can be safely imaged in almost all situations. There is an increasing body of literature describing the safety of imaging some cardiac pacemaker patients in a carefully monitored protocol. These preliminary results are exciting, and may expand the use of MRI but, imaging of patients with pacemakers is investigational and can not be recommended at this time.

Clinical Applications

Indications

A unique strength of magnetic resonance methods is the ability to obtain anatomic, functional and perfusion information with a single method. Vascular and nonvascular anatomy can be imaged with excellent resolution and, since MRI techniques are inherently 3 dimensional, images can be acquired in any plane. As long as the patient can cooperate with lying still and occasional breath-holding instructions (to reduce respiratory motion) high quality images can be obtained in most patients. Table 1 lists the current clinical uses for MRI. Resources are now available from international organizations which highlight clinical indications as well as appropriateness criteria.

<table>
<thead>
<tr>
<th>Table 1. Indications for cardiovascular magnetic resonance imaging assessment of right and left ventricular volumes, ejection fraction and mass</th>
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</thead>
<tbody>
<tr>
<td><strong>Ischemic Heart Disease</strong></td>
</tr>
<tr>
<td>(a) Ventricular morphology, volumes and ejection fraction</td>
</tr>
<tr>
<td>(b) Myocardial perfusion at rest and following pharmacologic stress</td>
</tr>
<tr>
<td>(c) Myocardial viability following contrast administration (delayed CE-MRI)</td>
</tr>
<tr>
<td>(d) Phosphorous spectroscopy (investigational – not a current clinical tool)</td>
</tr>
<tr>
<td><strong>Valvular Heart Disease</strong></td>
</tr>
<tr>
<td>(a) Serial assessment of ventricular volumes, ejection fraction and mass</td>
</tr>
<tr>
<td>(b) Valvular morphology (echo techniques are first line)</td>
</tr>
<tr>
<td>(c) Quantitative flow, measuring stenotic gradients and regurgitant fractions</td>
</tr>
<tr>
<td><strong>Myocardial Disease Primarily Involving the Left Ventricle</strong></td>
</tr>
<tr>
<td>(a) Ventricular morphology, volumes and ejection fraction</td>
</tr>
<tr>
<td>(b) Assessment of patterns of hypertrophy (hypertrophic cardiomyopathy)</td>
</tr>
<tr>
<td>(c) Delayed CE-MRI as an aid in recognizing the etiology of cardiomyopathy (e.g. dilated or ischemic cardiomyopathy, myocarditis, sarcoid, amyloid)</td>
</tr>
<tr>
<td><strong>Right Ventricular Cardiomyopathy</strong></td>
</tr>
<tr>
<td><strong>Pericardial Disease</strong></td>
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<tr>
<td>(a) Constrictive pericardial disease</td>
</tr>
<tr>
<td>(b) Atypical pericardial effusions (echo techniques are first line)</td>
</tr>
<tr>
<td><strong>Congenital Heart Disease</strong></td>
</tr>
<tr>
<td>(a) Morphology of the heart, central pulmonary arteries and aorta</td>
</tr>
<tr>
<td>(b) Right and left ventricular morphology and function</td>
</tr>
<tr>
<td>(c) Assessment of intracardiac shunts</td>
</tr>
<tr>
<td>(d) Assessment of post-surgical results</td>
</tr>
<tr>
<td><strong>Assessment of Cardiac and Paracardiac masses</strong> (echo techniques are first line)</td>
</tr>
<tr>
<td><strong>Diseases of the Thoracic and Abdominal Aorta</strong></td>
</tr>
<tr>
<td><strong>Peripheral and Cerebrovascular Angiography</strong></td>
</tr>
<tr>
<td><strong>Coronary Artery Imaging</strong></td>
</tr>
<tr>
<td>(a) Assessment of anomalous coronary arteries</td>
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<tr>
<td>(b) Kawasaki’s disease</td>
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</table>

Ventricular Function

Validation of the accuracy of MR methods for assessing volume, function and mass dates back to the early days of cardiovascular MRI. In the opinion of most authorities, MRI now represents the gold standard for assessing right
and left ventricular function. Unlike other modalities, MRI can accurately and reproducibly assess ventricular function and mass independent of geometric assumptions. In our lab, we routinely assess ventricular function using several single plane long axis images and a stack of serial short axis images proscribed to encompass the entire heart from base to apex. To acquire a 2 chamber plane (RAO equivalent), a 4 chamber plane (LAO equivalent) and an LVOT plane requires a total of 3 EKG-gated, breath-hold scans each lasting only ~5 to 10 seconds. Using these views, standard area-length ejection fraction calculations can be obtained which are quick and accurate, particularly in patients with normal regional wall motion. The serial short axis series usually requires 4 to 6 separate breath-hold scans. Accurate ejection fraction and volume calculations can be made using a Simpson’s rule algorithm. Results obtained using these inherently 3 dimension data sets are reproducible and accurate even in patients with regional wall motion abnormalities. A comprehensive assessment of ventricular function can be obtained in ~10 minutes from the time the patient lies down in the scanner until the results are obtained. MRI has the added benefit of being able to measure wall thickness, wall thickening and LV mass. Patients, such as those with chronic valvular pathology, in who chamber dilatation and ejection fraction influence prognosis and the timing of surgical intervention, can be accurately followed. The benefits of MRI can also be exploited in the research community, particularly in the area of drug therapy and development. Studies can be designed that involve fewer patients and can be accomplished in a more cost effective and shorter time frame using MRI methods.

**Cardiomyopathy**

MRI is useful for the assessment of patients with cardiomyopathy since treatment algorithms are often based on the etiology and severity of myocardial dysfunction. Defining an ischemic etiology may lead to additional testing in the hope of identifying treatable coronary artery obstruction. Accurate assessment of ejection fraction can influence the appropriate use of device therapy in the form of biventricular pacing and/or implantable defibrillators. Facilitating proper patient selection for device therapy is an issue of clinical and economic importance.

Contrast enhanced MRI (CE-MRI) techniques have been used to accurately distinguish between ischemic and nonischemic etiologies for cardiomyopathy. Patients with prior myocardial infarction (ischemic etiology) demonstrate a characteristic endocardial to transmural pattern of contrast enhancement following gadolinium infusion (see section on Ischemic Heart Disease). In comparison, patients with a nonischemic etiology typically do not show this pattern. In ground-breaking work from the laboratory of Dr. Dudley Pennell at the Royal Brompton Hospital in London, McCrohon et al. showed that patients with nonischemic dilated CE-MRI often demonstrate a pattern of mid-wall enhancement. Their work was the first to suggest that delayed CE-MRI may become a useful alternative to invasive coronary angiography in the work-up of patients with cardiomyopathy. This is a complicated and somewhat controversial area and continued research is to be expected.

Abnormal contrast uptake has been seen in patients with acute myocarditis using several acquisition techniques although the findings can be variable. Ventricular function assessment, chamber morphology, valvular function, quantitative flow measurements and CE-MRI make possible a comprehensive evaluation of known or suspected hypertrophic cardiomyopathy. Figure 3 is an example of asymmetric septal hypertrophy in a patient with hypertrophic cardiomyopathy. MRI may be uniquely useful in less common variants such as apical hypertrophic cardiomyopathy which can be missed by echocardiography. MRI findings in sarcoid and amyloid heart disease have been described by MRI, although the findings can be variable and nonspecific.

![Cardiomyopathy](image-url)

Figure 3. Basal slice from a cine MRI study demonstrating asymmetric septal hypertrophy in a patient with hypertrophic cardiomyopathy.

Cardiomyopathy associated with thalassaemia can be evaluated by MRI. These patients often receive multiple blood transfusions during their lifetime resulting in iron overload and cardiomyopathy with subsequent death due to arrhythmia or heart failure. There is no consistent relation between serum iron and myocardial dysfunction. Nor does liver iron consistently predict myocardial iron content. Some authors have demonstrated the usefulness of the MRI T2* studies in diagnosing such cases. It is hoped that diligent follow-up may prevent myocardial scarring and irreversible cardiomyopathy in this select population.

Right ventricular cardiomyopathy is difficult to evaluate...
and requires the combination of a strong clinical suspicion and the strict application of clinical and imaging criteria. Since the right ventricle is poorly evaluated by echo, nuclear and catheterization techniques MRI has assumed an important role in the imaging criteria. Helpful parameters include right ventricular dilation, focal contractile abnormality, trabecular disarray and fat infiltration of myocardium.

Ischemic Heart Disease

Left ventricular size and function is a major determinant of prognosis in patients with ischemic heart disease. As noted above, the accuracy of MRI for assessing both the myocardium (mass, wall motion, regional wall thickening) and the blood pool (chamber volumes and ejection fraction) is quite helpful. MRI pharmacologic stress testing can be performed using dobutamine or adenosine. The spatial resolution of MRI stress testing is superior to conventional nuclear studies but, stress testing in the MR environment can be cumbersome and therefore, is not widely used.

MRI can also be used to assess myocardial viability. The usual protocol includes assessment of cardiac anatomy and function and delayed imaging of the myocardium following the infusion of gadolinium contrast (delayed CE-MRI). The gadolinium chelates in routine clinical use are primarily extracellular agents which diffuse into the interstitial space. Normal myocytes exclude gadolinium while areas of myocardial scar, which don’t contain normal myocytes, accumulate gadolinium over time. When imaged with a specialized inversion recovery sequence normal myocardial tissue is nulled and made to appear dark (black). Figure 4 is an example of a normal delayed CE-MRI study.

In contradistinction, abnormal areas of high gadolinium concentration are made to appear bright (white). The easily remembered adage in MR myocardial viability imaging is: “bright is dead”. Figure 5 is an example of a localized myocardial infarction from our lab.

Valvular Heart Disease

Transthoracic and transesophageal echocardiography are excellent techniques for assessing fine morphologic detail of
heart valves. However, MRI is complementary for assessing valve morphology and, is a superior technique for assessing the physiologic consequences of valvular pathology. Subjective assessments can be obtained using cine gradient echo techniques which highlight the disturbed flow patterns characteristic of valvular stenosis and regurgitation. Reproducible objective assessments can be obtained using quantitative flow and volumetric MR techniques. Aortic and mitral valve gradients and valve areas can be rapidly calculated in a manner analogous to echocardiography. Reproducible objective assessments can be obtained using quantitative flow and volumetric MR techniques. Aortic and mitral valve gradients and valve areas can be rapidly calculated in a manner analogous to echocardiography.46-48 Regurgitant flow and volume can be reproducibly assessed in both mitral and aortic regurgitation.49-51 Magnetic resonance methods are uniquely helpful in identifying patients with pathology of the aortic valve and ascending aorta. It has been recognized that patients with a congenitally abnormal aortic valve (bicuspid) often have associated pathology of the aortic wall (aneurysm or coarctation). A high index of suspicion is required to tailor the diagnostic imaging strategy and guide appropriate therapy. In these patients, MRI is used to assess anatomy and ventricular function, quantitative flow methods are used to assess stenotic and/or regurgitant lesions and MRA is used to assess the entire aorta. Figure 6 is an example of a patient from our lab that was accurately diagnosed by MR methods and underwent successful surgical therapy.

Prosthetic valves can be imaged safely but, morphologic detail at valve level valve cannot be assessed due to local artifacts from the metallic components of the valves. Eccentric regurgitant jets and quantitative flow can still be assessed.

**Pericardial Disease**

MRI is accurate for diagnosing pericardial effusions. Echocardiography is the initial choice for assessing pericardial pathology but, MRI is complementary and is particularly useful for assessing loculated effusions. MRI can also contribute to the evaluation of suspected constrictive pericardial disease by allowing accurate measurement of pericardial thickness and assessment of the physiologic sequelae of constriction such as RV chamber distortion and RA enlargement. Calcium produces an MRI signal void and its presence can only indirectly be inferred by MRI. Computed tomography (CT) is another tool that can be used since CT very accurately assesses pericardial calcium content. A comprehensive assessment of pericardial disease often requires a multimodality approach.52

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Figure 6. MRI quantitative flow assessment in a patient with a bicuspid aortic valve and ascending aortic dilatation (circled region of interest in the bottom frames). The top left frame is a graphic representation of flow across the region of interest at the level of the aortic valve. The top right frame demonstrates volumes and flow velocities in tabular form. This patient was shown to have increased velocities and severe aortic regurgitation. He underwent successful replacement of his aortic root and aortic valve.
**Cardiac and Paracardiac Masses**

Echocardiography is the first line imaging strategy for evaluation of cardiac masses but MRI is an important complementary tool. The large field of view can precisely assess size and the relationship to cardiac and noncardiac structures. The flexibility of imaging sequences (e.g. T1-weighted, T2-weighted and fat suppression techniques) permits some insight into tissue composition. Finally, image appearance following contrast infusion facilitates assessment of vascularity. Left ventricular thrombi, even small apical thrombi, can be reliably imaged using MRI techniques (Figure 7).

![Figure 7. Cine MRI demonstrating a small apical thrombus (arrow)](image)

**Congenital Heart Diseases and Post Surgical Follow Up**

Advances in medical and surgical techniques have created an increasing population of patients with congenital heart disease surviving into adulthood. Echocardiography is an excellent tool in most young children. However, MRI is of great complementary utility in complex congenital heart anomalies in the adult. The absence of radiation or nephrotoxic iodine administration is important in the younger population. The wide field of view facilitates the systematic assessment of cardiac morphology as well as the status of venous return, the central pulmonary arteries and the thoracic aorta.6,53,54 Quantitative flow techniques can be used to noninvasively calculate systemic and pulmonary blood flow and, thereby identify the presence of any shunt. Figure 8 is an example of an atrial septal defect with a significant left-to-right shunt identified in our lab.

In the post-surgical population, surgically created conduits can be notoriously difficult to locate and interrogate. MRI is useful to follow patients after surgery and to look for complications or residual defects. The wide field of view of MRI and the ability to perform quantitative flow assessment in any imaging plane can be helpful.

![Figure 8. Cine MRI of a sinus venosus atrial septal defect (arrow). RA, Right atrium; LA, Left atrium](image)

**Coronary Artery Imaging**

A significant body of research has been done on MR coronary angiography and in carefully selected patients diagnostic images can be obtained. A preliminary early report was published many years ago by Dr. Warren Manning and associates comparing MR coronary angiography with conventional angiography.55 Figure 9 is an example of an MR coronary angiogram obtained in our lab. It must be recognized that the technical requirements are considerable and long acquisition times are required. Accordingly, MR coronary artery imaging is seldom used clinically in the detection of atherosclerotic coronary artery disease.

![Figure 9. MR coronary angiogram of a normal right coronary artery (arrows)](image)
A niche clinical use of MR coronary imaging is for the detection of congenital coronary anomalies involving the origin and course of the proximal vessels.\textsuperscript{56} In young patients, where the desire to avoid radiation is of greatest relevance, MRI is often used as the first line test. Coronary artery aneurysms, such as those seen in Kawasaki’s disease, can be followed-up via MRI (Figure 10). In the current state of development, CT coronary angiography is much faster, has superior spatial resolution and is the preferred noninvasive strategy for coronary imaging in most situations. Research using magnetic resonance to characterize not only the lumen of the epicardiac coronary arteries but to assess plaque morphology continues.

**Magnetic Resonance Angiography**

Magnetic resonance imaging is inherently sensitive to flow and early investigators recognized the potential for noninvasive MR angiography. The earliest efforts were done by manipulating imaging sequences in order to highlight natural flow phenomena and contrast. However, it wasn’t until the widespread use of MR contrast agents that MRA became sufficiently accurate and reproducible for clinical use. Magnetic resonance angiography has revolutionized the diagnostic evaluation of patients with aortic disease (Figure 11), renovascular disease (Figure 12), cerebrovascular disease, and upper and lower extremity peripheral vascular disease (Figure 13). In the past, most of these patients required invasive angiography to assess their status. Currently, in state-of-the-art labs, almost all diagnostic angiography is accomplished noninvasively with MRA or, recently, CT angiography. The invasive angiography suite remains valuable to arbitrate an equivocal or nondiagnostic noninvasive angiography study. Fortunately, the major role of the invasive angiography suite has shifted to the performance of therapeutic interventions.
Future Considerations

The field of cardiovascular magnetic resonance is well established for the clinical applications described above. This field is far from mature and new developments are being reported regularly. Accurate definition of atherosclerotic plaque composition and burden would be of enormous clinical utility and is an area of active and promising research. Work continues to be pursued in the area of MR coronary angiography. A potential role for MR spectroscopy has been described and is the subject of ongoing basic science investigation. The disciplines of interventional MRI and high field strength (3 Tesla) MRI are also in their early stages.

Conclusions

Magnetic resonance methods are assuming an increasingly prominent role in the evaluation of patients with cardiovascular disease. The contemporary clinician should acquire a working knowledge of the technology available and how to apply these techniques in a cost effective manner. It is to be expected that the uses of cardiovascular MR will proliferate as promising new avenues of research are explored.

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