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IMPORTANT ADVANCES IN TECHNOLOGY AND UNIQUE APPLICATIONS RELATED TO CARDIAC MAGNETIC RESONANCE IMAGING

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Abstract

Cardiac magnetic resonance has become a well-established imaging modality and is considered the gold standard for myocardial tissue viability assessment and ventricular volumes quantification. Recent technological hardware and software advancements in magnetic resonance imaging technology have allowed the development of new methods that can improve clinical cardiovascular diagnosis and prognosis. The advent of a new generation of higher magnetic field scanners can be beneficial to various clinical applications. Also, the development of faster acquisition techniques have allowed mapping of the magnetic relaxation properties T1, T2, and T2* in the myocardium that can be used to quantify myocardial diffuse fibrosis, determine the presence of edema or inflammation, and measure iron within the myocardium, respectively. Another recent major advancement in CMR has been the introduction of three-dimension (3D) phase contrast imaging, also known as 4D flow. The following review discusses key advances in cardiac magnetic resonance technology and their potential to improve clinical cardiovascular diagnosis and outcomes.

Introduction

Cardiac magnetic resonance (CMR) has become a well-recognized imaging modality and is viewed as the gold standard for myocardial tissue viability assessment, ventricular volumes, blood flow quantification, and cardiac function evaluation. It has also played a significant role in valve disease, although it usually acts as a second-line technique to assist when Doppler echocardiography has proven problematic due to limited acoustic access, highly eccentric jets, or the need for precise quantification.

While CMR has been used for tissue characterization and blood flow quantification in past decades, recent technological hardware and software advancements in magnetic resonance imaging (MRI) technology have allowed the development of new methods that can improve clinical cardiovascular diagnosis and prognosis.

1.5 Tesla vs 3 Tesla

Achieving higher resolution is always an aim for clinical and biomedical imaging. At present, cardiovascular imaging is making considerable advances toward fulfilling this requirement, mainly with the continued improvements in MRI hardware and software. Optimal diagnostic-quality MRI requires a balance among signal-to-noise ratio (SNR), tissue contrast, acquisition time, and spatial and temporal resolutions. Since the SNR is directly proportional to the magnetic field strength, increasing the field strength leads to an inherent improvement in SNR that can then be traded for improved spatial resolution, improved temporal resolution, or reduced acquisition time. In 1998, the U. S. Food and Drug Administration (FDA) approved the use of MRI systems up to 4 Tesla (T) to qualify as nonsignificant risk devices, which led the way for manufacturers to introduce the whole body 3-T scanners in addition to the typical 1.5-T scanners already in use. While 3-T MRI systems have been available for nearly 15 years, their use in CMR had been limited because CMR pulse sequences are highly sensitive to the field inhomogeneity artifacts. However recent improvements in field homogeneity and new advanced shimming techniques have propelled 3-T CMR.

There are several advantages in using the higher field strength scanners. A number of recent comparisons of pulse sequences at 1.5-T and 3-T have demonstrated close to the theoretical doubling of SNR in cardiac imaging applications in the higher field scanners.[1] Also, the introduction of parallel imaging,[2] with improved radiofrequency electronics and coil design, has facilitated the use of higher acceleration factors. All that led to improvements in the speed, resolution, and coverage of CMR imaging. Recently, several studies have highlighted the positive outcome when using contrast-enhanced magnetic resonance angiography with parallel imaging at higher field strengths.[3]

Besides the increase in SNR in higher field strengths, it has been shown that the T1 relaxation time (a measure of how quickly the net magnetization vector recovers to its ground state) increases with field strength by about 43% in myocardium and 34% in blood.[4] This increase can be an advantage in CMR depending on the imaging application. For example, spin labeling technique benefits from the longer T1 times at higher field strength and can be translated into better assessment of myocardial perfusion.[5] Viability imaging is another technique that benefits from the increase of T1 time at 3-T.[6] Since the relaxation time of paramagnetic contrast agents such as the commonly used gadolinium-based contrast is slightly reduced in 3-T field strength,[7] the increase in baseline tissue T1 time becomes an advantage when these T1-shortening paramagnetic contrast agents are used. This combination leads to a larger signal difference between contrast-enhanced tissue and blood/unenhanced surrounding tissue.

With all the above-mentioned advantages, there are some challenges in using 3-T over 1.5-T scanners. The electrocardiogram, which is essential to gating-based imaging, can be harder to

acquire at 3-T. Also, artifacts are more common and some restrictions may be necessary to limit heating effects from the radiofrequency energy.

T1, T2, and T2* Parametric Mapping

One of the most important developments in software and CMR pulse sequence design has been parallel imaging. It allows a robust method for accelerating image acquisition that has paved the way for parametric mapping of the magnetic relaxation properties T1, T2, and T2* in the myocardium. Faster image acquisition made the generation of these maps clinically feasible in a single breath-hold. In order to generate a relaxation map, multiple images of the same region of the myocardium are acquired with different sensitivities to the parameter of interest, and the signal intensities of these images are fit to a model that describes the underlying physiology or relaxation parameters. T1 mapping is performed before and after the administration of contrast, and measured values can then be used to calculate native T1 and extracellular volume (ECV) fraction in the myocardium. The amount of ECV in the myocardium correlates to the amount of diffuse myocardial fibrosis and myocardial infiltration.[8] T2 mapping can be used to measure myocardial edema and inflammation whereas T2* mapping provides an assessment of myocardial iron-overload and myocardial hemorrhage.

T1 Relaxation Time Mapping

Delayed enhancement CMR (DE-CMR) is the reference standard for assessing myocardial replacement fibrosis in ischemic and nonischemic cardiomyopathy.[9,10] DE-CMR images enable the visualization and quantification of myocardial infarction and replacement fibrosis. The infarcted regions have a slower washout rate of gadolinium contrast than healthy myocardium, leading to lower T1 relaxation times in these areas and creating a difference between normal and irreversibly injured tissue.

However, DE-CMR is unable to identify diffuse interstitial fibrosis. Recently, T1 mapping of the myocardium after the administration of gadolinium contrast has been shown to identify increased extracellular volume that occurs in the setting of diffuse interstitial fibrosis. There has been a growing interest in assessing ECV as a noninvasive biomarker for diffuse fibrosis, amyloidosis, and myocarditis.[11-13] Noninvasively assessing myocardial ECV by T1 mapping can assist in monitoring the effectiveness of therapies aimed at regressing myocardial fibrosis and even in early identification of patients at risk of developing heart failure. While endomyocardial biopsy can be prone to sampling errors and is limited by its accessibility to certain regions of heart, T1 mapping allows reproducible noninvasive sampling of the entire myocardium.

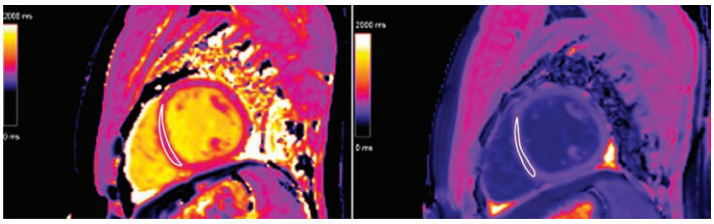

Figure 1. T1 mapping of a patient with ECV at 22.2%. (A) Precontrast T1 map of the myocardium (T1 in selected ROI is 1143 ms). (B) Postcontrast T1 map (T1 in selected ROI is 529 ms). ECV: extracellular volume; ROI: region of interest.

T2 Relaxation Time Mapping

T2 is the relaxation time for transverse magnetization. T2 values have been shown to increase in regions where edema and inflammation are present.[14] However, older techniques using black-blood sequences to measure the T2 relaxation times have significant limitations. The loss of signal in the myocardium through the heartbeat cycle during acquisition poses a major challenge. Another problem arises from the T2 sequence itself as it is nonquantitative in nature, and using multiple standard deviations to differentiate between the normal and abnormal myocardial segments could introduce an interpretation bias in defining what is normal versus abnormal.

Recent technological advances in image acquisition have enabled the generation of T2 maps. Similar to the T1 mapping, multiple images are acquired at the same location within the myocardium but with various T2 sensitivities. The multiple echo times acquired provide multiple points along the T2 relaxation curve for data fitting. The effects of signal loss or any coil inhomogeneities are eliminated during the curve fitting. Besides being used to detect the presence of edema and inflammation, T2 maps can be used in clinical settings to detect various cardiac pathologies including myocarditis and Takotsubo cardiomyopathy.[15] In that study, T2 mapping was shown to have 94% sensitivity and 97% specificity for identifying edema in the myocardium, while 30% of patients enrolled went undetectable using conventional direct T2 measurements.

T2 Relaxation Time Mapping*

T2* is the transverse magnetization relaxation time in the presence of magnetic field inhomogeneities. T2* relaxation time quantification is well established in CMR and is used to measure and monitor iron overload in the myocardium. T2* time is shortened by magnetic inhomogeneities introduced by the presence of iron depositions in the myocardium.

T2* time quantification is also used as an indicator for chelation therapy. Abnormal T2* values are considered the most important predictor of future need for chelation therapy. Change in T2* relaxation time has been taken into account as an end point in chelation therapy clinical trials.[16] T2* mapping can also assist in identifying myocardial hemorrhage in acute myocardial infarction.[17]

4D Flow

Another major recent advancement in CMR has been the introduction of three-dimensional (3D) phase contrast imaging, also known as 4D flow. Traditionally, CMR imaging of flow has been realized using methods that resolve two spatial dimensions (2D) in individual slices. This approach allows measurements of forward, regurgitant, and shunt flows in normal, congenital, and acquired heart disease.[18] However, such acquisitions require prospective appropriate placement of the velocity mapping plane and have limitations relative to the multiple directions of flow through the heart and large vessels.

Recent phase contrast CMR imaging allows for the acquisition of 3D morphology and time-resolved blood flow velocities in x, y, and z axes. With 4D flow sequence, one can acquire the anatomical and three-directional velocity information for each voxel within a 3D volume at all measured time points of a cardiac cycle. The temporal evaluation of flow can benefit from the isotropic higher spatial resolution that 3D offers. This allows for detailed quantitative flow and vessel wall parameters with complete volumetric coverage and overcomes the limitations in

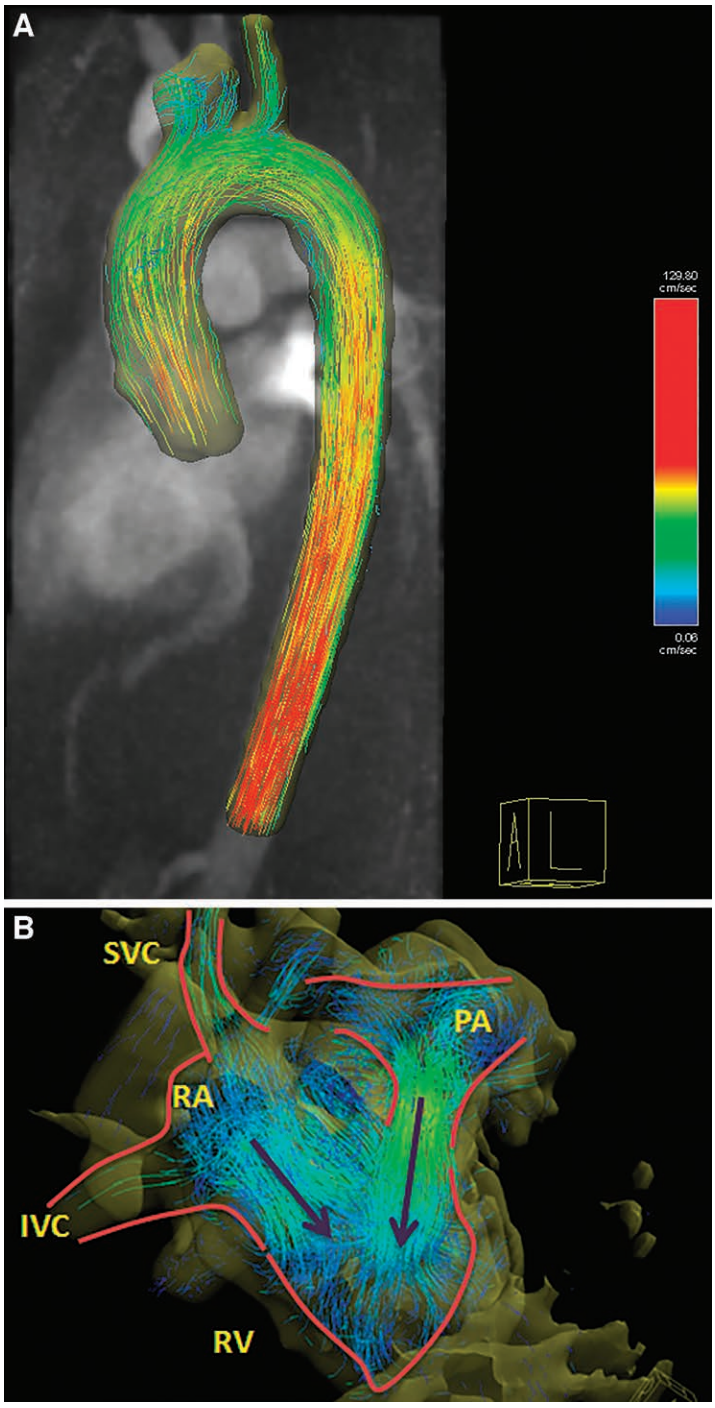

Figure 2. (A) Streamlines of the 4D flow within a normal aorta and (B) diastolic flow pattern in a patient with severe pulmonary regurgitation. Regurgitant flow from the pulmonary artery is directed toward the RV apex. Inflow from the right atrium is also directed to the apex. SVC: superior vena cava; IVC: inferior vena cava; RA: right atrium; RV: right ventricle; PA: pulmonary artery.

nonuniform flow quantification from 2D flow imaging. Another advantage of 4D flow is the ability to retrospectively select any individual planes for analysis of velocities. However, in the past the acquisition of these very large datasets took time and relied on efficient synchronization relative to cardiac and respiratory movements that often limited its use.

Modern technological and methodological improvements such as parallel imaging and more efficient respiratory control have allowed the acquisition time of 4D datasets to drop to reasonable scan times of approximately 8 to 15 minutes. These advances have made it feasible to use 4D flow imaging to acquire comprehensive flow information within reasonable time. Various analysis and data processing software packages have been introduced for the visualization and quantification of flow and other parameters from the acquired datasets.

The collected raw image data are a time-resolved 3D volume of velocity vectors. This data is imported into a 3D visualization software program (e.g., GTFlow, EnSight). There exist several ways to present the 4D flow data including individual velocity vectors, streamlines, and particle traces. The individual vectors are used to show the velocities at the level of a selected plane. Even though this is the simplest representation of a 4D flow set, the individual vector tracing usually does not describe complex 3D flow patterns well. Streamlines and particle traces are used to demonstrate complex flow patterns such as helices and vortices. Streamlines and particle traces are imaginary lines that depict the local velocity field at a specific point in time and the path an imaginary particle would take over time, respectively. Using the analysis tools, it is possible to calculate different parameters from an extracted 2D plane such as velocity profile, flow volumes, and peak and average velocities.

Recently, there have been numerous studies that show the potential of using 4D flow imaging across different cardiovascular disciplines. The first application of 4D flow has been to visualize complex flow patterns in the thoracic aorta that are associated with healthy versus pathologic hemodynamics.[19-21] Multiple flow patterns have been noticed in ascending aortic aneurysms and aortic dissections.[22-23] Another area that has received attention using 4D flow is the quantification of intracardiac blood flow and visualization of flow patterns within the cardiac chambers. New studies have emerged employing 4D flow in the left and right ventricles to assess and integrate flow patterns with morphological changes.[24,25] This can lead the way to a better understanding of the different flow patterns in various congenital heart abnormalities.

Conclusion

The introduction of 3 Tesla clinical scanners as well as advances in both software and sequence and coil design have proven beneficial in cardiac magnetic resonance imaging. The gain in signal-to-noise ratio from using a high field strength magnet appears to lead to improvements in contrast-enhanced methods such as first-pass perfusion, delayed enhancement, and magnetic resonance angiography. Also, these technical improvements have brought about quantitative techniques for myocardial parametric mapping of magnetic relaxation times. These maps can extend the unique potential of CMR for characterization of cardiac structure and physiology. However, further research will be necessary to show the incremental diagnostic and prognostic usefulness and robustness compared to current CMR techniques. Lastly, the increasing versatility of CMR, its 3D nature, and its unique capabilities have proved to be increasingly important in assessing 4D flow patterns in various vascular and cardiac abnormalities.

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