**Talk Title:** Comprehensive Cardiac MRI: Technical

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**HIGHLIGHTS**

- Cardiac MRI must assess morphology, function, blood supply, and tissue status
- Cardiac MRI scans must be gated to the heart cycle
- Gated scans also typically require some form of respiratory correction
- Morphology and function are often assessed simultaneously with a cine scan
- Blood supply to the heart is assessed by monitoring the passage of contrast agent through the myocardium
- Myocardial tissue status can be assessed with a “late enhancement” technique,

**OVERVIEW**

The objective of cardiac MRI is to assess the health status of the heart. To perform a complete assessment, different aspects of the heart must be examined: First, the morphology of the heart must be assessed. In many cardiac diseases, the physical appearance of the heart may be altered. Second, a characterization of cardiac function must be performed. Since the primary function of the heart is to pump blood, an assessment of heart’s ability to contract and relax is required. The third aspect of the heart that must be examined is its blood supply. A number of different cardiac pathologies may arise if this is compromised. Finally, the status of the myocardial tissue itself must be examined. In particular, we want to determine if the myocardial tissue is alive, dead, or structurally altered.

The above discussion describes the information that cardiac MRI is required to provide in order to establish the basic health of the heart. However, the heart is an organ that presents some particular challenges for MRI. Specifically, unlike other organs, the heart is in constant motion. This motion is due to both cardiac contraction as well as respiration. The time scale of these motions is generally on the same order as the time required to form an MR image. As a result, the heart will generally be in different orientations over the course of an MR data acquisition. If not accounted for, these variations in orientation will lead to inconsistencies in the MR data. In turn, these inconsistencies will give rise to errors (or “artifacts”) in the MR images reconstructed from this data. Thus, to effectively image the heart, the issue of cardiac and respiratory motion must be addressed.
In the sections below, basic techniques used to image the heart with MRI will be discussed. Following this, an overview of MRI methodology utilized to assess the basic properties of the heart (morphology, function, blood supply, and tissue status) will be presented.

**BASIC CARDIAC MRI TECHNIQUES**

In a typical MRI scan, a 2D matrix of "k-space" data is acquired. However, the entire 2D matrix is not acquired at once. Rather, each 1D line of the matrix is acquired sequentially in time. After all data has been acquired, a Fourier Transform is applied to the 2D k-space data matrix to generate an image of the anatomy. The amount of time necessary to acquire a complete 2D matrix is given by:

\[
\text{Time to Acquire Full 2D Matrix} = \text{(Time to acquire single line of data)} \times \text{(Number of lines of data in 2D matrix)}
\]

In a typical scan, it may take about 5ms to acquire a single line of data, and there are typically around 200 lines of data in the 2D matrix. Inserting these numbers into the above formula implies that about 1 second is required for MR data acquisition. If one is imaging static structures (e.g. brain, knee, etc.) then this does not present a problem. However, in the case of the heart, an issue arises. In particular, the heart contracts and relaxes approximately once a second. Therefore, over the course of a one second MR data acquisition, there will be significant differences in the morphology of the heart. These morphological changes will lead to inconsistencies in the data. In turn, this will cause errors (or "artifacts") in the reconstructed image that can significantly degrade diagnostic quality.

To deal with the problem of cardiac motion, the data acquisition is "gated" to the cardiac cycle. This means that, rather than acquiring data continuously over time, the data acquisition is instead synchronized to the patient's cardiac cycle. This is accomplished by monitoring the patient's electrocardiogram (ECG) signal during the MR scan. Following the detection of the peak ECG signal (i.e. the R-wave), a small portion of k-space data is acquired. By keeping the amount of k-space data acquired small, there will effectively be no motion during the data acquisition period. On subsequent cardiac cycles, this process is repeated to acquire the remaining k-space data. Thus, while cardiac motion occurs continuously, the heart is effectively "frozen" during the time in which data acquisition occurs. As a result, the heart is in a consistent position during data acquisition, and cardiac motion-related artifacts are minimized. The time delay between the R-wave and the commencement of data acquisition (also known as the "trigger" delay) determines the position within the cardiac cycle that the image will portray. For example, if data acquisition is delayed for 700ms following the R-wave, then the resulting image will reflect the heart at a time point 700 ms into the cardiac cycle.

The above discussion illustrates how gating can minimize motion artifacts related to cardiac motion. However, the use of gating comes at a cost in terms of efficiency. In particular, since data acquisition only occurs during a small portion of the cardiac cycle, the total amount of time required to acquire the full k-space data set is correspondingly increased. For example, if data acquisition occurs in only 10% of the cardiac cycle, then the total time required to acquire all k-space data will be increased by a factor of 10! Using the numbers from the example given above, if a continuously acquired MR scan requires...
about 1 second to complete, then a gated scan would therefore take about 10 seconds. Aside from the direct inconvenience of reduced efficiency, the increased scan time associated with gating leads to another problem: respiratory-related motion artifacts. If an MR scan of the heart persists for much longer than a second, then the heart will undergo significant motion due to respiration (i.e. breathing). If not addressed, this respiratory motion will lead to motion artifacts.

By far the most common method to deal with respiratory motion is to have the patient to hold their breath for the duration of the scan. When successful, this virtually eliminates respiratory-related motion artifacts. However, there are two major limitations with a breath holding approach: First, many patients, especially those with morbidities, are unable to hold their breath for the required duration. Second, even in healthier individuals, there is a limit to breath hold duration. This places an upper limit on how much k-space data may be acquired in a scan. In general, the amount of k-space data acquired is directly linked to a number of important image properties (e.g. spatial resolution, FOV, SNR). Therefore, breath holding places an upper limit on the achievable image quality. In recognition of these limitations, a number of "free-breathing" cardiac imaging techniques have been developed. Most of these techniques monitor respiratory motion in some manner. This information is then used to identify a set of k-space data that was acquired during periods of minimal respiratory motion. The drawback with a free-breathing approach is that, since only data acquired during minimal respiratory motion is utilized, some data must by definition be rejected. As a result, the overall data acquisition efficiency is reduced, and scan time consequently increased. The most common free-breathing method is the "navigator echo". This technique monitors respiratory motion with a separate MR acquisition of the diaphragm.

In a gated MR scan, a small amount of k-space data is acquired during a specific phase of the cardiac cycle. The length of time over which this occurs is called the data acquisition "window". The size of the window (which is a parameter that can be controlled by the user) determines how much k-space data can be acquired in each cardiac cycle; the larger the window, the more data that can be acquired. For example, if the window is doubled from 30ms to 60ms, then twice as much k-space data may be acquired per cardiac cycle. The advantage of a larger window is that fewer cardiac cycles are then necessary to acquire the full k-space data set. This in turn reduces the overall scan time. In patients who have difficulty holding their breath, increasing the window is one method that can be used to reduce the required breath hold duration. However, recall that the purpose of acquiring only a small amount of k-space data per cardiac cycle is so that there is little cardiac motion during this time period. Therefore, if the window is set too large, significant motion may occur, and motion artifacts may result.

CARDIAC MORPHOLOGY/FUNCTION

Morphology refers to the physical form and structure of the heart, whereas function refers to the heart’s ability to contract and relax. For diagnostic purposes, cardiac morphology and function are intimately related. In many cardiac diseases, changes in morphology will subsequently give rise to changes in cardiac function. For example, a pathological thickening of the myocardium can sometimes
impede the heat's ability to contract. Conversely, some morphological changes only become apparent when examining cardiac function. For example, some pathological changes in myocardial thickness may only be visible during certain phases of cardiac contraction. Therefore, a large portion of cardiac MR diagnosis relies on a simultaneous examination of cardiac morphology and function. This is accomplished through the acquisition of a "cine" cardiac MR scan. In a cine scan, a series of images are produced at sequential stages of the cardiac cycle. When played consecutively, these images provide a movie of the heart throughout the cardiac cycle. In the movie loop, both morphology (e.g. wall thickness, structural abnormalities) as well as function (i.e. ability to contract and relax) may be assessed.

A cine data acquisition represents a direct extension of the gated MR technique given. In the previous section, it was shown how the trigger delay determines the position within the cardiac cycle that the image will portray. However, there is no reason why one must be restricted to just a single data acquisition period. In fact, one may acquire the same portion of k-space data repeatedly throughout the cardiac cycle. In this manner, the data associated with each acquisition period (called a "segment") will be acquired at a different phase of the cardiac cycle. If the data from each segment is reconstructed into a separate image, each image will represent a different phase of the cardiac cycle. If these individual images are played out sequentially, a movie loop of the cardiac cycle will be generated.

One important property of a cine MR scan is its "temporal resolution". This is defined as the length of time between image frames in the movie loop. The temporal resolution governs how accurately motion may be depicted. If the temporal resolution is too coarse, then the movie will appear "choppy". In this case, it may not be possible to accurately visualize the contraction and relaxation of the heart. The temporal resolution of the scan depends on the length of the data acquisition window. For example, if the data acquisition window lasts for 50ms, this means that every image in the cine loop will be separated by 50ms. Thus, as the window is increased, the temporal resolution gets worse.

Cine MR is used to assess morphology and function. However, a number of different pulse sequences may be acquired in cine mode. In cardiac MRI, by far the most common cine pulse sequence is steady state free precession (SSFP, also called TrueFISP, Balanced FFE, and Fiesta). SSFP is similar to a gradient echo sequence. However, unlike a gradient echo, all gradient waveforms are balanced such that at the end of each TR, the gradients do not impart any net phase. Moreover, unlike gradient echo, magnetization is not spoiled on each TR.

The most unique feature of SSFP is that, unlike almost all other pulse sequences, tissue contrast is largely independent of the pulse sequence parameters; especially TR and flip angle. This fact has a number of consequences which make SSFP attractive for cardiac MRI: First, while the tissue contrast is independent of flip angle, the signal-to-noise ratio (SNR) increases with flip angle. As a result, large flip angles may be used to produce high SNR, without any concomitant loss of tissue contrast (as is the case with other pulse sequences, such as gradient echo). In fact, the SNR of SSFP is often limited by specific absorption rate (SAR) considerations, rather than the magnetization physics. A second attractive feature of SSFP is that, since tissue contrast is independent of TR, the TR's can be made very short (~3ms is typical) without any change in tissue contrast or SNR. As a result of the short TR, the overall
SSFP scan time tends to be relatively short. In fact, the TR of SSFP is typically limited by gradient switching and/or receiver bandwidth considerations, rather than physics of the magnetization. As a result of the above properties, SSFP images are typically produced with high SNR (due to the large flip angle) and relatively short scan times (due to the short TR). This combination is ideal for cardiac MRI. There are, however, a number of disadvantages with SSFP. First, the fixed tissue contrast of SSFP may not necessarily be optimal for visualizing all aspects of the anatomy and/or pathology. In this case, other pulse sequence or modifications to the basic SSFP pulse sequence may be required. A second disadvantage of SSFP is the presence of “banding artifacts”. These artifacts are dark lines which pass through the image. These lines are due to inhomogeneities in the magnetic field. Such banding artifacts may be particularly prominent (and obstructing) when metallic objects (e.g. wires) are present.

**BLOOD SUPPLY TO THE HEART**

The heart's primary purpose is to pump blood out to the tissues of the body. The myocardial tissue itself, of course, is no exception. In order for the myocardium to remain healthy, it requires an adequate supply of blood. In general, the blood supply to the heart can be assessed at two levels: The first is at the large vessel coronary artery level. Significant stenoses of these vessels will restrict blood supply to the heart. Unfortunately, accurately characterizing coronary stenoses requires a spatial resolution that is currently beyond the capability of most MR acquisitions. As a result, except for select research sites, direct MR coronary angiography is rarely performed. The second type of myocardial blood supply assessment is at the level of capillary "perfusion". While challenging, assessing perfusion with MRI can be performed as part of a routine clinical protocol. One additional point that should be noted is that most perfusion MR scans must be performed at rest and at stress. Imaging at stress greatly increases the sensitivity of perfusion MRI, as many stenoses are not flow-limited at rest.

The basic methodology for assessing perfusion with MRI involves monitoring the passage of contrast agent through the myocardium. However, there are many different methods for assessing this information. In general, these methods can be classified as; quantitative, semi-quantitative, and qualitative. In a quantitative assessment, mathematical operations are applied to the signal-intensity time curves in each pixel. These operations provide the absolute perfusion in terms of flow/volume at every location in the myocardium. While attractive from the standpoint of providing an absolute, patient-independent assessment of perfusion, quantitative methods have very strict requirements in terms of data quality (e.g. spatial/temporal resolution, SNR, etc.). As a result, fully quantitative methods are not widely used. At the other end of the spectrum, in a qualitative analysis, the MR images as a function of time are simply monitored visually. The objective is to visually detect the presence of any abnormalities in the contrast agent kinetics as it passes through the myocardium. While this approach has the advantage of simplicity, it is often lacks sensitivity and robustness. It may also sometimes be difficult to distinguish pathological changes in perfusion from a variety of artifacts that may arise during scanning. Semi-quantitative methods apply some sort of mathematical operation to the signal-intensity time curves in each pixel. These operations generally do not directly provide an absolute quantification of perfusion (like fully quantitative methods). Instead, one is typically interested in using the
mathematical metrics produced by these techniques to discriminate healthy from pathologic myocardium. For example, one common semi-quantitative method assesses the maximum slope of the signal-intensity time curve at each pixel of the myocardium. Semi-quantitative methods provide some level of robustness and sensitivity over simple qualitative methods.

To accurately image perfusion with MRI, the pulse sequence must meet a number of stringent requirements. First, it must acquire images fairly rapidly (every 1-2 heartbeats). This is necessary to accurately visualize the contrast agent as it passes through tissue. Conversely, images must be acquired with sufficient spatial resolution in order to visualize subendocardial defects, as well as to assess the transmural extent of pathology. At the same time, the pulse sequence must acquire a sufficient number of slices to cover the heart volume. Additionally, for best results, it is often necessary to fully follow the complete passage of the contrast agent through the myocardium. This often requires an extended period of time that may last close to a minute of scanning. A final requirement relates to the SNR and “linearity” of the contrast agent signal. Basic perfusion theory relates blood flow through the myocardium to the change in contrast agent concentration. However, MR imaging does not measure contrast agent concentration directly, but rather indirectly through its effect on the signal. In general, linearity between signal intensity and contrast agent concentration typically occurs only at lower concentrations. Conversely, to achieve good SNR, high contrast agent concentrations are desired. Therefore, a tradeoff between these two requirements is often necessary.

There is a large number of different pulse sequences used for perfusion imaging. Below, we will focus on one of the simpler ones, gradient-echo echo-planar imaging (GRE-EPI) with saturation recovery. This will be used to illustrate some of the basic properties required of a perfusion imaging pulse sequence. The pulse sequence begins with a 90° non-slice-selective saturation pulse, followed by a short delay. The purpose of this is to introduce a T1-weighting into the signal. With this weighting, the signal intensity will increase with decreasing T1 value, and therefore with increasing contrast agent concentration. A 90° saturation pulse is used rather than a more conventional 180° inversion pulse for two reasons: First, the delay period required for T1 weighting with saturation recovery is relatively short. As a result, there isn’t a lot of “dead time” during the pulse sequence. Secondly, because the magnetization is saturated (i.e. zeroed), this provides some insensitivity to arrhythmias, which may otherwise cause beat-to-beat variations in signal intensity. Following the delay period, the magnetization signal must be recorded. To meet the need for acquiring an image every 1-2 heartbeats, this readout must occur relatively rapidly. Therefore, a fast GRE-EPI readout is used. To further shorten the data required for each image, partial Fourier and/or accelerated imaging techniques are often used. To cover the volume of the heart, the acquisition described above is typically repeated multiple times per heart beat for different slices. The disadvantage of this approach is that different slices will be at different phases of the heart cycle. However, this penalty is often accepted in the interests of a significantly more efficient acquisition. Finally, as mentioned earlier, image may be acquired repeatedly for close to a minute to provide a complete assessment of perfusion. This relatively lengthy scan time is beyond the capacity of a breath hold for most people. Therefore, images acquired at a later time may be misregistered to earlier images. For a quantitative analysis, it may be necessary to register these images prior to analysis.
TISSUE CHARACTERIZATION

In a variety of cardiac diseases, the status of the myocardial tissue itself may be altered. In particular, it may be dead, alive but non-functional, or structurally altered. An accurate assessment of the status of the cardiac tissue provides critical diagnostic and prognostic information. A complete characterization of the myocardial tissue requires multiple tests. However, one single test that provides information in a surprising number of cardiac pathologies is the “late enhancement” technique. In this technique, a Gd-based contrast agent is injected intravenously. After a delay period of about 10 minutes, T₁-weighted imaging is performed. In both infarction and a wide range of cardiomyopathies, the presence of pathological tissue is indicated by an increased signal. Under normal circumstances, Gd cannot enter into the interior of myocytes. However, in acute myocardial infarction, cells lose their membrane integrity. As a result, contrast agent may enter into the interior of infracted cells. Under these circumstances, the relative volume occupied by Gd will be larger in infracted tissue than in healthy tissue. Infarcted tissue is therefore brighter on a T₁-weighted image than healthy tissue. In chronic infarction as well as a number of cardiomyopathies, healthy myocytes are replaced by fibrous tissue. The fibrous tissue occupies a smaller relative volume than the myocytes which they replaced. Therefore, contrast agent in this tissue will therefore occupy a relatively larger volume, which can again be detected as increased signal on a T₁-weighted image.

The basic late enhancement pulse sequence begins with a 180° inversion pulse. This is followed by a delay time (called the inversion time, or TI). For maximum sensitivity, TI is chosen to null signal from normal myocardium. This ensures a maximum contrast between healthy and pathological tissue. Following the delay period, the k-space data is encoded. Many possible acquisition schemes have been proposed. For example, one of the simplest is a gradient echo readout. Data is typically recorded only at a single phase of the heart cycle -- typically in diastole to minimize motion artifacts. In most implementations, a breath hold is used to minimize respiratory motion. It typically takes multiple breath holds to acquire enough slices for complete volumetric coverage of the heart.

The key factor that determines the sensitivity of the late enhancement technique is the degree to which the normal myocardium is nulled by the 180° inversion pulse. In turn, this is determined by the choice of TI time. However, the appropriate selection of the inversion time is not necessarily trivial. The reason for this is because of the length of time required to complete the entire late enhancement scan. Each breath hold and patient recovery period may take up to a minute. Assuming a total of 10-15 slices, the total time required for full volumetric coverage could be in the range of 10-15 minutes. During this period, the contrast agent concentration, and therefore the T₁ value, changes. As a consequence, even if the inversion time is selected correctly at the beginning, it may not be correct later on due to the changing T₁ values. To compensate for this, it is typical to vary the inversion time as one acquires subsequent slices. There are also so-called “phase-sensitive” late enhancement methods which are much more robust across a range of inversion times. However, the cost of these scans is that they typically take longer to perform.