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Real-Time Cardiac MRI Without Triggering, Gating, or Breath Holding

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Abstract

State-of-the-art cardiac MRI can perform real-time 2D scans without cardiac triggering during a single breath hold; however, real-time cardiac MRI in rats is difficult due to the high heart rate (330 bpm) and presence of respiratory motion. These challenges are overcome by using a dynamic imaging method based on Partially Separable Function (PSF) theory with an acceleration factor of 256. This paper demonstrates that this method can be used in the study of transplanted rat hearts for both anatomical and perfusion applications. The study was carried out with a 200 μm in-plane resolution with a 17.2 msec temporal resolution, and the results show improved spatial resolution (2x) and reduced acquisition time (3x) relative to Electrocardiogram (ECG) triggered, respiratory gated cine imaging.

Introduction

Cardiac MRI is a powerful tool capable of measuring anatomical structure, left ventricle ejection fraction, myocardial mass, muscle contraction, flow velocity, first pass perfusion, delayed contrast enhancement, blockage of arteries, and cellular and molecular processes [1], [2]. The state-of-the-art in cardiac MRI using fast pulse sequences, parallel imaging, and dynamic imaging combined with cardiac triggering can achieve non-real-time 3D scans in a single breath hold [3] and real-time 2D scans without cardiac triggering [4] (also see [1], [5] for recent reviews).

Real-time imaging not only enables perfusion imaging. It provides a number of advantages including shorter scan times, robustness to arrhythmia, reduced sensitivity to patient motion, and operate without ECG and respiratory signals. These features increase patient comfort, broaden the applicability of MRI, and reduce the cost associated with the scan time.

Recent results in cellular and perfusion MRI demonstrate that acute and chronic rejection of transplanted hearts can be detected [6], [7]. The application of real-time imaging to the analysis of acute transplanted heart rejection directly impacts the science by reducing experiment time, improving spatial resolution, and enabling the simultaneous study of perfusion and immune response.

If real-time MRI can be extended to 3D and used in the analysis of acute transplant rejection, then many additional impacts exist. Obviously the perfusion analysis can be extended to 3D and correlated with the immune response via labeled cells. Full heart characterization of the response of patient specific immune suppression therapy also becomes possible, and these results can lead to a non-invasive method to complement biopsy. Finally, a CT-like scan

prescription and data analysis paradigm is possible and would simplify the practical use of cardiac MRI since there would no longer be a need to prescribe a double-oblique slice to view the short-axis of the heart.

Real-time MRI in transplanted rat hearts is challenging because of the heart rates (330 bpm), respiratory motion (1 Hz), spatial resolution (200 μm), and low SNR. These difficulties have been addressed by using non-real-time gated cine (Electrocardiogram (ECG) triggered, respiratory gated) imaging with multiple averages [6]. This technique significantly reduces motion artifacts, but it still suffers from long scan times, limited spatial resolution, and inability to perform perfusion imaging.

This paper demonstrates that real-time imaging technology based on sparse sampling can be used in the study of acute rejection of heart transplants. The results show successful anatomical imaging with better quality and lower scan time than gated cine as well as a perfusion study comparing native and non-rejecting, transplanted hearts (isografts).

Theory and Methodology

Theory

The real-time imaging method used here uses a Partially Separable Function (PSF) model of the data and a specially designed sampling pattern in the k - t space. Conditions for exactly representing the dynamic image space by the M^{th} order separable function in Equation 1 have been established [8].

$$\rho(\vec{x}, t) = \sum_{m=1}^M c_m(\vec{x}) \varphi_m(t) \quad (1)$$

This model can be transformed to the k - t space as shown in Equation 2 where α_m is the Fourier transform of c_m .

$$d(\vec{k}, t) = \sum_{m=1}^M \alpha_m(\vec{k}) \varphi_m(t) \quad (2)$$

The PSF model and cardiac MRI data redundancy enables the use of the k - t sampling pattern given in Figure 1. The Cartesian k - t space sampling pattern in Figure 1 is designed such that two scans are interleaved: (1) high spatial, low temporal resolution data (solid red dots) referred to as $d_{\text{img}}(\vec{k}, t)$ and (2) low spatial, high temporal resolution data (blue circles) denoted $d_{\text{nav}}(\vec{k}, t)$. The requirements for the sampling pattern are as follows:

- $2T_R$ must satisfy the temporal Nyquist rate ($d_{\text{nav}}(\vec{k}, t)$).
- Δk_y must satisfy the spatial Nyquist rate ($d_{\text{img}}(\vec{k}, t)$).
- $N \geq M$ sampling frames must be collected ($d_{\text{img}}(\vec{k}, t)$).

Experimental Conditions

All experimental data in this paper were collected using a Bruker (Billerica, MA) Avance DRX 4.7 T, 40 cm equipped with a 12 cm, 40 G/cm shielded gradient set. A 5.5 cm custom built surface coil was used for the collections.

Also, all the PSF data collections used customized FLASH pulse sequences at 256×256 resolution over a 5×5 cm Field of View (FOV) with a 2 mm slice thickness. The T_R was 8.6 msec, and T_E was 4 msec. $N = 128$ sampling frames were collected to overcome the limited SNR of the collected data (resulting in a 10 minute data acquisition time), and $M = 16$ model order was used in the reconstructions.

The PSF data were collected continuously without respiratory gating. The collections were started by an ECG trigger to allow for repeatable timing of the contrast injection; however, experiments performed with arbitrary starting times provided equally good reconstructions. ECG recordings show mild variations in the cardiac cycle; however, the respiration cycles are very stable since the rats were anesthetized using a small animal ventilator.

The animals used in the study were the same type of Dark-Agouti and Brown Norway rats as in reference [6]. All animals received humane care in compliance with the *Guide for the Care and Use of Laboratory Animals*, published by the National Institutes of Health, and the animal protocol was approved by the Carnegie Mellon University Institutional Animal Care and Use Committee.

Real-Time Cardiac Imaging

Comparing the gated cine images to the PSF reconstructions in Figure 2 shows that the gated images are generally more blurry due to the averaging over the respiratory gating window and slight aperiodicity of the heartbeat. The isograft heart is an extreme example where the ECG and respiratory signals were not especially clean. The gated cine image appears almost like a simple average over time, and the detailed anatomical features are not clear.

The blurriness of gated cine can be reduced at the expense of a longer scan time by reducing the respiratory gating window; however, the ultimate limit is still determined by the quality of the data selection and the repeatability of the underlying physiology. In these experiments the gated cine data required a variable amount of time between 20 and 40 minutes to collect versus the consistent 10 minutes for the PSF method.

The data in Figure 2 show representative results from proof-of-concept contrast injection experiments. Two types of rats were used in these experiments: (1) rats with native hearts, (2) rats with genetically matched transplants (isografts). The images show that the geometric structures present in these two types of animals varies greatly, because the transplanted heart is placed in the abdomen. The region surrounding the transplanted heart shows the largest anatomical variation since its placement is not reliable.

Figure 3 demonstrates the temporal resolution of the PSF reconstruction. The PSF reconstruction provides a faithful distinction between the diastole and systole phases of the heartbeat. It succeeds even though practically every organ in the FOV is moving due to respiration.

Also, the quality of the reconstructions is vastly improved over the Fourier method applied to the time sequential samples, $d_{\text{img}}(\vec{k}, t)$. The motion artifacts of the heart region from the cardiac and respiratory motion are outlined by the blue box in Figure 3, and they are suppressed to a great degree. The PSF method is performing temporal interpolation in a situation where the temporal Nyquist criterion is not satisfied, because the basis has less unknowns than the number of measurements.

Discussion

Imaging Characteristics

The temporal basis functions are determined using a Principle Component Analysis (PCA) [8]. The $d_{\text{nav}}(\vec{k}, t)$ data are arranged in a matrix, D_{nav} , where each column contains the temporal samples of a unique location in the k space. Then the PCA is formed.

$$D_{\text{nav}} = U \sum V^H \quad (3)$$

The first M columns of U are taken as the temporal basis, $\{\phi_m(t)\}$. Then these basis functions are fit to the measured data, $d_{\text{img}}(\vec{k}, t)$.

The k space basis functions are computed by separately solving Equation 4 at each point in the k space, so it should be clear that Cartesian sampling is not a requirement for using this method. The temporal basis functions, $\{\phi_m(t)\}$, were interpolated to the sample times in $d_{\text{img}}(\vec{k}, t)$ using cubic splines, and their values were placed into the $\Phi(\vec{k})$ matrix. There are M unknowns and N measurements for each point in the k space, and the solutions presented in this paper were regularized using a truncated SVD matrix inverse. The spatial basis functions, $c_m(\vec{x})$, are then the inverse Fourier transforms of the collection of $\alpha_m(k)$.

$$\arg \min_{\vec{\alpha}(\vec{k})} \left\| \vec{d}_{\text{img}}(\vec{k}) - \Phi(\vec{k}) \vec{\alpha}(\vec{k}) \right\|_2^2 \quad (4)$$

The dynamic images were reconstructed using Equation 1 for computational efficiency since the transformation from the k space to the spatial domain only needs to be performed M times instead of at every point in time. The reconstruction of $\rho(\vec{x}, t)$ at any time, t_0 , can then be expressed as the weighted sum of M time invariant images, $\{c_m(\vec{x})\}$, where the weights are $\{\phi_m(t_0)\}$.

The model order, M , can be chosen by truncating the singular values based on the noise level in the data. Calculations show that an M chosen this way result in a model order over 30; however, in this research the model order has been selected to truncate negligible basis function coefficients in addition to those corresponding to noise ($M = 16$). Simulations show a mild smoothing in the temporal domain is the dominant effect of this compression.

When the temporal basis function matrix, $\Phi(\vec{k})$, is ill-conditioned, the noise is amplified for an entire line of the k space. This condition can occur when M is too high and creates artifacts that appear similar to traditional motion artifacts. Ill-conditioning can also occur due to unlucky sampling of the basis functions, so randomized temporal sampling might be thought to solve the issue. However, evenly distributing the temporal samples of $d_{\text{img}}(\vec{k})$ throughout the experiment has proven to be the most reliable approach. Most importantly, the side effect of ill-conditioning looks similar to traditional motion artifacts, so it can be easily identified.

When M is slightly too low, the temporal curves are smoother, and the edges of the image are poorly tracked. At first they become blurred ($M = 12$), and as M decreases to around 8 the effect is like a double edge at the interface of the blood pool and myocardium. In these cases it can sometimes be difficult to determine if the method has failed or not, because the artifacts can be unusual.

Extremely low M in the 1 to 4 range give high noise suppression, because there are fewer unknowns. The reconstructions tend to appear very clean and often not blurry, but there are almost no meaningful temporal characteristics in the data. The low noise, high spatial resolution appearance of these images can appear correct especially since average cardiac images are blurry in the regions with motion. However, an examination of the singular values of D_{nav} quickly shows that these low model orders are not appropriate.

In most cases it is necessary to choose a model order above the knee of the singular value curve to avoid image artifacts. In these experiment the knee of the curve is around $M = 8$, and a value of $M = 16$ was used. Increasing M beyond this value results in reconstructions with more noise that do not track the dynamic changes with any more accuracy.

Experimental results for the spatial and temporal basis functions are shown in Figure 4 ($M = 16$ and $N = 128$). The spatial basis functions decay in magnitude as m increases, and this behavior is expected because of the decay of the singular values of D_{nav} . Each spatial basis in Figure 4(a) is modulated by the corresponding temporal basis function in Figure 4(b) to form the reconstruction. The spatial basis functions can be interpreted as assigning spectral energy groups to image pixels.

The temporal basis functions in Figure 4(b) are zoomed to show two respiratory cycles, and the lower order functions are quasi-periodic. The basis functions are orthogonal by definition of the PCA, and they are normalized to have a total energy of 1. The first basis function dominates the DC spectral term since cardiac images are dominated by large semi-static organs, and the higher order basis functions generally have higher bandwidths.

Future Work

The extension of MRI to real-time, 3D cardiac imaging is fundamentally limited by the amount of data that can be collected during the allowed experiment time, T_{exp} . All MRI data are collected time sequentially, so only a finite amount of data, N_{exp} , can be collected during T_{exp} . Fast pulse sequences, strong magnetic field gradients, and fast analog to digital converters can only push the performance so far until patient safety and T_2^* decay limits are reached.

The problem of real-time, 3D cardiac imaging reduces to determining where to collect and how to use the N_{exp} samples to reach the desired spatial and temporal resolution given the SNR of the data, so the implication is that imaging techniques enabling sparse sampling are essential to achieving this goal. For the SNR observed here, 128 samples for each k space point over time are required for the PSF method, and the result is an acceleration factor of 256.

Conclusion

Real-time imaging has been successfully applied to the imaging of native and transplanted rat hearts. The anatomical imaging clearly distinguishes the diastole and systole geometries of the heart cycle, and the functional perfusion data are similar to others in the literature.

The PSF method provides an improvement in the spatial resolution (2x) and experiment duration (3x) over gated cine imaging, and the technique will allow questions involving blood flow in acutely rejecting hearts to be answered. Also, the high performance of the PSF method suggests that it can be extended to 3D with a great impact on cardiac MRI.

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Fig. 1.
The k - t sampling pattern used for 2D Cartesian phase encoding.

Fig. 2.

A comparison between native and transplanted (isograft) rat hearts. Perfusion of a Gadolinium contrast agent can be tracked using the PSF method. The PSF images also have higher spatial resolution than the gated images though both have the same number of spatial encodings (256×256).

Fig. 3.

The temporal resolution of a transplanted rat heart with respiratory motion. The PSF method suppresses motion artifacts, provides high temporal resolution, and accurately tracks the heart geometry even though nearly every organ in the FOV is moving due to respiration.

(a) Spatial Basis

(b) Temporal Basis

Fig. 4.

The first 4 of 16 spatial and temporal basis functions for a transplanted rat heart. (a) The images are independently scaled, and their magnitudes generally decrease as m increases. (b) Only two respiratory cycles are shown.