Published in final edited form as:

Magn Reson Med. 2010 August ; 64(2): 501–513. doi:10.1002/mrm.22444.

Patient-Adaptive Reconstruction and Acquisition in Dynamic Imaging with Sensitivity Encoding (PARADISE)

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Abstract

MR imaging of the human heart without explicit cardiac synchronization promises to extend the applicability of cardiac MR to a larger patient population and potentially expand its diagnostic capabilities. However, conventional non-gated imaging techniques typically suffer from low image quality or inadequate spatio-temporal resolution and fidelity. Patient-Adaptive Reconstruction and Acquisition in Dynamic Imaging with Sensitivity Encoding (PARADISE) is a highly-accelerated non-gated dynamic imaging method that enables artifact-free imaging with high spatio-temporal resolutions by utilizing novel computational techniques to optimize the imaging process. In addition to using parallel imaging, the method gains acceleration from a physiologically-driven spatio-temporal support model; hence, it is doubly accelerated. The support model is patient-adaptive, i.e., its geometry depends on dynamics of the imaged slice, e.g., subject's heart-rate and heart location within the slice. The proposed method is also doubly adaptive as it adapts both the acquisition and reconstruction schemes. Based on the theory of time-sequential sampling, the proposed framework explicitly accounts for speed limitations of gradient encoding and provides performance guarantees on achievable image quality. The presented in-vivo results demonstrate the effectiveness and feasibility of the PARADISE method for high resolution non-gated cardiac MRI during a short breath-hold.

Keywords

Cardiac MRI; Non-gated; Model-based; Patient Adaptive; k-t Sampling; Sensitivity Encoding

1. Introduction

The physiological motion within the imaged slice in two-dimensional (2D) cardiac MR imaging (CMRI) is very fast relative to the image acquisition speed of conventional MR schemes for imaging static objects (1). Modern CMRI protocols use fast pulse sequences and parallel imaging to speed up acquisition. Parallel imaging techniques such as SENSE (2), usually reduce the number of phase encoding steps to accelerate the acquisition, and compensate for the reduced Fourier encoding by exploiting the multi-channel spatial encoding provided by the phased-array receivers. In addition, electrocardiogram (ECG) gating is typically used to synchronize the acquisition to cardiac motion. However, as it

acquires multiple cardiac phases over several heartbeats, such synchronized segmented k-space imaging disregards the beat-to-beat motion variation and essentially assumes that the cardiac cycle is periodic. Therefore, the underlying condition for accurate gated imaging is a regular cardiac rhythm, which is violated in case of arrhythmia, commonly present in a significant portion of cardiovascular patients with left ventricular (LV) dysfunction and heart failure (3). The difficulties of obtaining high-quality ECG gating in MRI scanners also cause several practical disadvantages, e.g., reduction in the overall clinical throughput due to increased exam complexity (4). Moreover, in some cases accurate ECG referencing may be infeasible, e.g., in patients with abnormal chest geometry or those with low voltage ECGs (5).

In the absence of synchronization, however, even higher speedups are required to achieve a desirable *spatio-temporal (S-T) fidelity*—defined as a measure of how closely the reconstructed motion matches the true dynamics of cardiac tissue. Although state-of-the-art CMRI techniques enjoy accelerated MR signal encoding using a combination of parallel imaging and fast pulse sequences, in non-gated imaging such techniques alone are typically insufficient for achieving simultaneous high S-T resolutions and high S-T fidelity (6,7) for the following reasons: (i) limitations on gradient encoding performance; and (ii) limitations on parallel imaging acceleration due to the associated “geometric factor” (g-factor) signal-to-noise ratio (SNR) penalty (2). Consequently, there has been significant interest to move beyond such limits by devising highly accelerated acquisition and model-based reconstruction schemes (8–13).

Conventional non-gated techniques (i.e., with no cardiac synchronization), using a sliding window (or view-sharing) along the temporal dimension (14), have been shown to be capable of analyzing global cardiac function within a breath-hold (15,16). However, a major factor influencing the accuracy of global ventricular volume evaluations and confidence in wall motion assessments is the temporal resolution, which is desired to be at most 50 ms for resting heart-rates (17,18), and better for stress conditions. To illustrate the associated difficulties, consider a 2D imaging scenario with temporal resolution of 60 ms, and image matrix of size 200 along the phase-encode (PE) direction using a balanced steady-state free-precession (bSSFP) pulse sequence with 3 ms repetition time (TR). The acquisition of a full frame every 60 ms would require an acceleration factor of 10 or more. Providing such an acceleration using parallel imaging alone would incur extremely high g-factors. This highlights the magnitude of the challenge in achieving high spatial resolution (1–2 mm) while maintaining desirable temporal resolution and acceptable image quality using available non-gated techniques—especially for patients with a large-sized chest.

In this work, we approach the 2D dynamic imaging problem as a 3D reconstruction task with time treated as an independent dimension, hence the notion of 2D+t imaging. In order to achieve perfect S-T fidelity to the underlying *time-varying image* (TVI), i.e., to the imaged slice in 2D dynamic imaging, certain sampling density requirements must be met. The Nyquist criterion for 2D+t imaging involves sampling rate requirements in the joint k-space and time domain, here referred to as the *k-t space* (8,19,20). These sampling requirements are related to the model (*a priori* knowledge) assumed for the TVI, which expresses the redundancy in dynamic MR data resulting from the S-T correlations of the imaged slice. With this point of view, there is an arsenal of techniques for accelerated CMRI, referred to as model-based, constrained, reduced encoding, or prior-knowledge driven imaging (21). Examples include Keyhole (22), RIGR (8), DIME (9), and others (23,24).

According to multi-dimensional sampling theory, sampling in k_y -t space where k_y is the PE direction, results in aliasing of the signal spectrum in the reciprocal domain, i.e., the domain

that is dual to the k_y - t space (19,25). This domain is sometimes called the x - f space; here we refer to it as the y - f space. A significant class of CMRI techniques invoke the notion of compactness or sparsity of the signal support in the y - f space. For the dynamic imaging problem, a y - f support model identifies the locations where the signal is expected to have non-negligible energy in y - f space (19,25,26). The class of CMRI-suited techniques that are related to the notion of support modeling can be roughly categorized as follows:

- I. Generic (non-adaptive) modeling of the y - f support: Typically known as reduced field-of-view (FOV) techniques, methods such as UNFOLD (10) exploit the localization of the time-varying portion of the imaged slice to a fraction of the overall FOV (27,28). TSENSE (11) and UNFOLD-SENSE (29) combine elements of UNFOLD with parallel imaging.
- II. Statistical modeling of S-T correlations (12,13): The method of k - t BLAST and its multi-channel counterpart k - t SENSE, model the TVI's S-T correlations in the form of approximate second-order statistics.
- III. Sparse support modeling in a transform domain: These methods model the TVI as having a sparse (but generally unknown) support in a transform domain (30–33).
- IV. Adaptive sparse support modeling (34–39): The prior information in this class is adapted to the dynamics of the imaged slice and is in form of a y - f -space support model, called the dual- k - t support in previous work (36–38) and here, the *adaptive- y - f support*.

The method proposed in this work, dubbed Patient-Adaptive Reconstruction and Acquisition Dynamic Imaging with Sensitivity Encoding (PARADISE) (37–39), falls into the last category. The method owes its acceleration to (i) parallel imaging; and (ii) sparsity of the adaptive- y - f support model. Hence it is *doubly accelerated*. In addition, it is *doubly adaptive* as it adapts *both* acquisition and reconstruction to the support model (and in some versions (38,39) also to the specific coil sensitivities). Furthermore, the support model itself is physiologically-driven and subject-specific.

The PARADISE k - t acquisition scheme is unconventional because it is designed to prospectively guarantee the following desirable properties for the image reconstruction stage (Section 3.1):

- [P.1] Perfect unmixing (unaliasing) of the y - f -space signal is feasible—implying that subject to the modeling assumptions, the reconstructed cine would contain no aliasing distortion;
- [P.2] The cost of the unmixing task, i.e., the associated g-factor (SNR penalty) is minimized—thereby enabling high reconstruction SNR.

To achieve these properties, which ensure high S-T fidelity in the reconstructed cine, all available degrees of freedom inherent in the k - t sampling pattern are exploited so that the k - t acquisition is simultaneously, (i) adapted to the physiologically-driven y - f support; and (ii) optimized based on properties of sensitivity encoding in the y - f space. Furthermore, unlike previous methods except (9) and (34–36), PARADISE explicitly accounts—*both* in acquisition and reconstruction—for the time it takes to acquire each k - t sample (PE line in Cartesian imaging), namely, for the “time-sequential” constraint (19,25,40).

The aim of the proposed technique is to enable highly-accelerated non-gated CMRI with high S-T resolution and fidelity with the goal of providing insights into cardiac dynamics for diagnostic or basic research purposes. The presented work describes the theory and provides in-vivo results for the proposed method with comparisons to gated CINE and non-gated TSENSE methods.

2. Theory

The imaging goal is to reconstruct a 2D+t TVI denoted by $I(x,y,t)$ with high *Spatio-temporal (S-T) fidelity*. S-T fidelity is inversely proportional to the reconstruction error, defined as the root-mean square of the difference between $I(x,y,t)$ and the reconstructed cine¹ (i.e., the TVI within the time-span of the scan). In this section, we describe the theory for both data acquisition and image reconstruction stages of the proposed imaging method, as applied to 2D breath-hold imaging. Throughout the paper, k_y denotes the PE direction.

2.1. Dynamic MR Acquisition: Time-sequential k - t Lattice Sampling

Most dynamic imaging methods assume a k - t sampling pattern similar to the one shown in Fig. 2a, in which the time-sequential constraint mentioned in Section 1 is ignored. However, a more accurate representation of Cartesian k - t acquisition accounts for the time it takes to acquire a single PE (19,40). An example is shown in Fig. 2b, where a single PE is acquired per TR (9,25). The acquisition scheme in PARADISE is explicitly time-sequential (as in Fig. 2b) and is further restricted to a sheared grid in the k - t space with a fixed TR, called a “ k - t lattice” (Fig. 2c).

In Cartesian 2D+t imaging, all time-sequential *sampling schedules* can be described as $\Psi = \{(k_y[m], m \text{ TR}) \text{ for } m = 1, \dots, N_T\}$, where $k_y[m]$ is the only k_y location ($|k_y| \leq k_y^{\max}/2$) sampled at time $t = m\text{TR}$ and N_T is the total number of data samples acquired during the scan. We consider sampling schedules that lie on a k_y - t lattice Λ , defined as the set of points (k_y, t) whose coordinates satisfy $[k_y, t]^T = A\vec{n}$ for some 2-by-1 integer vector $\vec{n}$ and a 2-by-2 *basis matrix* A .

Based on the unified theory of time-sequential lattice sampling (19,40), a sampling schedule will satisfy the time-sequential constraint and have a fixed TR if its basis matrix has the following form:

$$A = \begin{pmatrix} k_y^{\max} & j_\Lambda \times \Delta k_\Lambda \\ 0 & \text{TR} \end{pmatrix}, \quad [1]$$

where parameters Δk_Λ and j_Λ determine the PE spacing (step size) and the subsampling factor in the k - t grid, respectively. In Fig. 2d, conventional k - t sampling (time-sequential) is shown overlaid on a k - t grid corresponding to this formulation (see the caption for details). Fig. 2e shows a generalized (PARADISE-type) time-sequential k - t lattice with Δk_Λ smaller than that in Fig. 2d (hence the denser grid). The spacing of consecutive PEs is given by $j_\Lambda \times \Delta k_\Lambda$ (with $j_\Lambda = 7$ in Fig. 2e). Comparing Figs. 2d and 2e, it can be seen that the generalized k - t lattice in Fig. 2e provides an additional degree of freedom for the k - t sampling pattern.

2.2. The Adaptive-y-f Support Model

The adaptive-x-y-f support model (Fig. 1), denoted by $\mathbb{B}$ captures the following characteristics of the energy distribution of the TVI in the x - y - f space (25,34–36):

- The TVI vanishes outside the finite spatial FOV.
- Highly dynamic motion is spatially localized to a dynamic FOV (dFOV) and temporally correlated. The temporal correlation is in form of *approximate* periodicity, implying concentration of signal energy around harmonics (integer

¹We use the term “cine” to refer to image sequences generated by non-gated schemes, while uppercase “CINE” will refer to images corresponding to an ECG-gated k-space scan.

multiples) of the average heart-rate (HR), f_{avg} . This feature is incorporated in the adaptive-x-y-f support as disks located at integer multiples of f_{avg} , which are called “model-bands.” The non-zero temporal bandwidth Δf of the model-bands allows for capturing beat-to-beat motion variability including aperiodicity. The highest temporal frequency included in the support model is denoted by f_{max} (Fig. 1).

- Motion outside the dynamic region is slow relative to the fast dynamics of the dFOV, hence modeled as a single large disk covering the entire FOV (Fig. 1). The allocated width Δf for this larger disk allows the support model to capture the slow dynamics of organs outside the dFOV, especially motion due to respiratory drift during a breath-hold scan.

Fig. 3 depicts a transverse slice of a realistic dynamic cardiac-torso numerical phantom, NCAT (41,42), representing the TVI in the spatial x-y domain. The cylinder overlaid on the dFOV along the f dimension corresponds to the higher dynamic energy content within dFOV and the bright-colored disks show the model-band locations. In order to demonstrate the banded nature of the energy distribution along the f dimension, we have plotted the 1D energy spectrum of the NCAT phantom (spectral analysis of a 20 second heart movie) with constant HR of 60 beats per minute (bpm). Note the very high concentration of signal energy at the harmonics (multiples of $f_{\text{avg}} = 1$ Hz). The effect of a varying HR or other forms of aperiodicity in the cardiac phantom is to spread the harmonic energy along f (35) as shown in the same plot for an aperiodic (time-warped) version of the NCAT phantom (42). The arrows in Fig. 3 establishing the correspondence of model-band locations to the 1D spectral energy plot, illustrate the notion of a multi-banded support capturing most of the signal content even for non-periodic TVIs. The effect of residual signal energy lying outside the support, is discussed in Section 5.4 (36,43).

It is known that sampling on a lattice Λ in k_y - t space (Section 2.1) results in aliasing of the signal in the reciprocal domain, i.e., the y - f space². The aliasing pattern is specified by a lattice Λ^* in the y - f space that describes the corresponding point spread function (PSF), called the “PSF lattice.” The aliasing is equivalent to convolution of the y - f signal with the following PSF:

$$h(y, f) = \frac{1}{|\det(A)|} \sum_{\vec{n}} \delta_D \left(\begin{bmatrix} y \\ f \end{bmatrix} - A^* \vec{n} \right) \quad [2]$$

where the summation is over all 2-by-1 integer vectors $\vec{n}$, $\delta_D(\cdot)$ denotes the 2D Dirac delta function, $A^* = (A^{-1})^T$ with T denoting the matrix transpose operation is the basis matrix for Λ^* and $\det(A)$ is the determinant of A (19).

Since the aliasing (described by the PSF in Eq. [2]) occurs in the y - f space, we will restrict our attention to the y - f -space counterpart of our adaptive-x-y-f support, denoted by B and called the adaptive-y-f support. The adaptive-y-f support B is the projection of B from the x - y - f space onto the y - f space, as described in Fig. 4a (36). This figure also shows a detailed view of B indicating its various parameters.

The notion of y - f support model can be applied to other well-known CMRI schemes as well—in particular to UNFOLD (26). Compared to UNFOLD (Fig. 4b), the structure of the adaptive-y-f support for PARADISE is sparser. As noted in Section 1, an important feature

²Owing to the almost instantaneous sampling (with Nyquist spacing) along readout k_x , an inverse Fourier transform along k_x decouples the analysis to each x location. Therefore, the k_x and x dependence is dropped from all functions.

of the PARADISE scheme is that, unlike UNFOLD, which uses a single fixed support, the geometry and dimensions of the adaptive-y-f support are physiologically-driven and subject-specific.

2.3. The PARADISE Inverse Problem

Recall that the adaptive-y-f support B indicates where the signal energy is located in the y - f space; hence, it can be used to determine the aliasing pattern corresponding to the PSF in Eq. [2]. Fig. 5a depicts aliasing of B on the PSF lattice by showing its main replica centered at the origin overlapping with another replica of B shifted to a grid point of the PSF lattice. The signal overlap due to aliasing in the y - f space (Fig. 5a) can potentially be unmixed using sensitivity encoding and prior information of the adaptive-y-f support B (Fig. 4a). Since the TVI $I(y, f)$ in y - f space has negligible energy outside B , the unmixing task is limited to points in B . We therefore introduce a mathematical description of this particular form of aliasing.

For a point (y_0, f_0) inside the adaptive-y-f support, i.e., for $(y_0, f_0) \in B$, consider the set of all points within the set B that overlap onto (y_0, f_0) due to the replication of B on the PSF lattice (Fig. 5a). This set will be called the *equivalence class* (EC) of (y_0, f_0) (37). It follows from Eq. [2] that the EC of (y_0, f_0) is given by

$$Q(y_0, f_0) = \left\{ \begin{bmatrix} y \\ f \end{bmatrix} \in B : \begin{bmatrix} y \\ f \end{bmatrix} - \begin{bmatrix} y_0 \\ f_0 \end{bmatrix} \in \Lambda^* \right\} \quad [3]$$

This point set can be graphically constructed by centering the PSF lattice at (y_0, f_0) and finding the lattice points that lie in the support B ; two instances of ECs are depicted in Figs. 5b and 5c.

It can be shown that the set of points of B is partitioned into such disjoint ECs. The global overlap pattern for the points of B can then be decomposed into independent patterns, each associated with a small unmixing subproblem. Transforming the data from all receiver coils to the y - f space produces the data vector $\vec{d}(y, f)$. The underlying inverse problem for recovery of the points in the EC $Q(y_0, f_0)$ can then be written in matrix form as (37):

$$\vec{d}(y_0, f_0) = \frac{1}{|\det(A)|} S_{Q(y_0, f_0)} \vec{T}_{Q(y_0, f_0)} \quad [4]$$

where $\vec{T}_{Q(y_0, f_0)}$ is a vector containing the unknowns $I(y, f)$ at points $(y, f) \in Q(y_0, f_0)$, and $S_{Q(y_0, f_0)}$ is the forward matrix containing the coil sensitivities (each row corresponding to a coil) computed at y -locations of the same EC. Eq. [4] is referred to as the *PARADISE equation*.

3. Methods

3.1. Acquisition Design Scheme

As explained in Section 2.3, the reconstruction task is to *unmix* the overlaps in y - f space for all points within the adaptive-y-f support. The matrices involved (Eq. [4]) and hence the reconstruction noise depend on the structures of all ECs. Given the desired spatial resolution (i.e., $1/k_y^{\max}$), from Section 2.1 it follows that the *degrees of freedom* in controlling the ECs are the following parameters of the k - t lattice Λ : (i) sampling interval TR; (ii) lattice subsampling factor j_Λ ; and (iii) Δk_Λ , the lattice grid-size along k_y . The goal of the acquisition design scheme is to optimally exploit these degrees of freedom to design a time-

sequential sampling schedule (Section 2.1) that ensures high S-T fidelity in the reconstructed cine. To achieve this, we search for a time-sequential k - t lattice that is adapted to the y - f support and optimized so that it possesses the two properties ([P.1] and [P.2]) introduced in Section 1.

It is possible to devise an optimal acquisition design scheme that requires the knowledge of coil sensitivity profiles (37–39). However, to enable fast and low-complexity design of the k - t sampling schedule immediately prior to running the MR scan, here we employ a purely “geometric” algorithm. This design algorithm is based on the geometry of overlap patterns in the y - f space and does not require any knowledge of the specific coil sensitivity profiles, relying instead on their generic properties.

For standard (volumetric) parallel imaging, it has been demonstrated that the g-factor can be improved by prudent design of the k-space sampling pattern: the aliasing can be “controlled” in two (spatial) dimensions so that sensitivity variations provided by the parallel coils can be optimally exploited to provide improved image quality (44). However, a different scheme is needed here since: (i) the aliasing domain is the 2D y - f space (rather than the 2D spatial domain); (ii) the time-sequential sampling constraint should be satisfied; and (iii) prior knowledge of the adaptive- y - f support must be taken into account. None of these aspects is present in (44). The details of the acquisition design algorithm are beyond the scope of the present article; but a high-level sketch of the scheme is provided in a recently presented abstract: (45).

3.2. Image Reconstruction

Fig. 6 summarizes the key steps in the proposed reconstruction algorithm; some details are provided in the caption. Following the unmixing, the reconstructed cine (TVI in y - t space) is obtained by an inverse temporal Fourier transform. Note that all the cine reconstruction steps are computed for a discrete grid in the 2D+ t space; and the solution (37) does not involve any regularization.

3.3. Imaging Experiments

MRI exams were performed on 1.5T Siemens Espree and Avanto whole body scanners (Siemens Healthcare; Erlangen, Germany) with 100 T/m/s and 200 T/m/s maximum gradient slew rates, and 33 mT/m and 40 mT/m maximum gradient amplitudes, respectively. Studies were performed under a protocol approved by the Institutional Review Board of the National Heart, Lung, and Blood Institute (NHLBI) and written informed consent was obtained from all study participants. Normal human volunteers (N=4) were scanned (2 male, 2 female; mean age: 44, range: 30–54 years; mean weight: 84.5 kg, range: 54–113 kg) with varying scan specifications (average HR range during scan: 53–72 bpm; range of breath-hold duration: 12–20 beats; range of HR variability during breath-hold: ± 5 bpm). For each PARADISE experiment, a different adaptive- y - f support was determined. Therefore, optimization of the pulse sequence prescription for each y - f support led to different scan settings and parameters for each subject and for each experiment. The presented scan details in this section and the results in Section 4 correspond to one particular, but typical, imaging experiment on the Avanto scanner (32 channels) using a 32-element cardiac-torso coil array.

Initially, CINE imaging during a single breath-hold using a retrospectively ECG-gated segmented bSSFP scan (TR/TE: 3.54 ms/1.77 ms, flip angle: 60°, receiver bandwidth: 558 Hz/pixel, views-per-segment: 4, total acquisition time: 19 s, average HR: 65 bpm) with rate 4 parallel imaging was performed in double oblique short-axis orientation with acquisition of one slice (7 mm slice thickness; approximately at mid-ventricle). The size of the FOV was 420mm×420mm (sized to avoid wrap-around along the PE direction). The FOV size/

location, slice thickness/location, and flip angle were kept constant for all subsequent scans. The image matrix size (readout $\times$ PE) was 256 $\times$ 224 resulting in an in-plane spatial resolution of 1.64 mm $\times$ 1.88 mm. Using GRAPPA rate 4 parallel imaging (32 reference lines), retrospectively-gated images were reconstructed (using the automated, standard scanner reconstruction) resulting in a temporal resolution of 14.2 ms, which is beyond the 30 ms threshold typically considered to be the desirable temporal resolution for cardiac cine imaging (46).

Next, two non-gated breath-held TSENSE scans were performed. The TSENSE scheme uses UNFOLD-type interleaved k - t sampling patterns so that high-quality estimation of coil profiles would be feasible every few frames (11). TSENSE with acceleration rate of R combines the acquired PEs from every R adjacent frames to achieve a single fully-encoded frame ($1/R$ temporal resolution). In our TSENSE implementation, we average all such fully-encoded frames (for the entire scan) to obtain a set of high SNR images for each coil. Next, an eigenvector-based coil profile estimation technique based on the work by Walsh et al. (47) is utilized (Personal Communication with Dr. Peter Kellman, NHLBI, NIH; August 2008).

The first TSENSE experiment had an acceleration rate of $R=2$ (TR/TE: 2.89 ms/1.45 ms, receiver bandwidth: 704 Hz/pixel, total acquisition time: 16.6 s, average HR: 66.1 bpm) with matrix size (readout $\times$ PE) of 192 $\times$ 192 (in-plane spatial resolution: 2.19 mm $\times$ 2.19 mm, temporal resolution: 277 ms) and the second scan had an acceleration rate of $R=5$ (TR/TE: 3.09 ms/1.55 ms, receiver bandwidth: 698 Hz/pixel, total acquisition time: 17.4 s, average HR: 62.3 bpm) with matrix size (readout $\times$ PE) equal to 256 $\times$ 223 (in-plane spatial resolution: 1.64mm $\times$ 1.88mm, temporal resolution: 138 ms). Furthermore, for estimation of the cross-channel noise covariance matrix, an integrated noise-only acquisition was conducted during the first 30 TRs by turning off the RF excitation (48).

PARADISE Pulse Sequence—A customized bSSFP pulse sequence was developed to allow for operator-defined TR and ordering of PEs, capable of acquiring a general k - t lattice. The pulse sequence included a user interface for inputting the lattice parameters (TR, Δk_{Λ} , j_{Λ}) and the number of k - t samples to acquire.

MR data for the PARADISE acquisition scheme with an image matrix size (readout $\times$ PE) of 256 $\times$ 220 (in-plane resolution: 1.64mm $\times$ 1.91mm) was collected during a short breath-hold (TR/TE: 3.09 ms/1.55 ms, receiver bandwidth: 698 Hz/pixel, total acquisition time: 12.46 s, average HR: 64.1 bpm). This acquisition was specifically optimized for the imaging experiment described below.

The scan was non-gated, however the ECG signal was recorded (in synchrony with the scan) for validation purposes. As in the TSENSE experiments, an integrated noise-only scan was performed.

Coil sensitivity estimates were derived using the same technique described for the TSENSE experiments hence eliminating the need for any extra calibration scan³. To verify the accuracy of the resulting coil sensitivity estimates, we implemented a short (2.47 s) coil calibration acquisition (128 symmetric PEs acquired 6 times sequentially) immediately prior to the k - t lattice. This alternative “reference” calibration scheme produced closely matching coil sensitivity estimates and no detectable change in the reconstructed images, validating the proposed calibration scheme.

³Also avoids misregistration between the calibration and accelerated scan. Further, since the coil profiles do not change appreciably during the breath-hold scan, dynamic updating of the coil profiles would not noticeably affect the results.

PARADISE Model Estimation—Fig. 7 provides an overview of the implementation stages involved in the proposed PARADISE acquisition design scheme, including the adaptation method for the adaptive-y-f support model. Here, we describe the procedure used for estimating the support parameters (Fig. 4a) from the available auxiliary information.

The dynamic FOV size and location was estimated using images from the initial short-axis localizer scans to determine the heart position within the chest, which for the described experiment was centered along the PE direction with a size of $0.4 \times \text{FOV}_y$. The average HR determining the f_0 parameter can be prospectively estimated from peripheral pulse or ECG signal observed during a breath-hold prior to the PARADISE scan. In our experiments, we used the average HR during the initial breath-hold gated scan ($f_{\text{avg}}=1.08$ Hz equivalent to 65 bpm). The actual HR during the PARADISE scan—measured using the independently recorded ECG—varied between 62 to 66 bpm with an average of 64.1 bpm.

The f_{max} parameter indicates the degree of temporal fidelity of the reconstructed cine to the underlying TVI. We postulate that having $f_{\text{max}} \approx 5f_{\text{avg}}$ would be sufficient for capturing the cardiac dynamics (including the rapid mid to end-systolic wall motion) with high S-T fidelity and no detectable image artifacts. This claim is validated empirically and demonstrated in Section 4 (Fig. 10). This choice of f_{max} implies that the adaptive-y-f support included 5 model-bands on each side of the DC ($f=0$) band, for a total of 11 bands (the exact f_{max} value is $5f_{\text{avg}} + \Delta f/2$).

The thickness of model-bands Δf reflects both the HR variability and potential misestimation of the average HR during the scan. The larger the chosen Δf , the greater the robustness to these effects, at the cost of reduced support sparsity—which in turn would imply reduced acceleration, increased g-factor, or a combination thereof. In the current implementation, we choose Δf based on a computational procedure—similar to the one sketched in Section 3.1—to obtain a low g-factor and hence excellent SNR (i.e., as good as or better than the gated scan). The result was $\Delta f = f_{\text{avg}}/3$, corresponding to a model-band thickness in Fig. 4a that fills 33% of the inter-band gap.

PARADISE Scan—Using the estimated adaptive-y-f support, the acquisition design scheme (Section 3.1) was executed to find the g-factor-optimized k - t lattice. As shown in Fig. 7, the implemented non-gated scan was a continuous k - t data acquisition prescribed by the PARADISE-designed lattice (total scan time: 12.46 seconds). The computation time for the acquisition design stage was less than 30 seconds (on a portable PC with 1.8 GHz Intel Pentium M processor and 1.5 GB of memory). The overall acceleration for the described PARADISE scan (discussed in Section 5.4) is a factor of 8.6 relative to the Nyquist criterion for 2D+t imaging (36,37).

Reconstruction was performed off-line on a standard 16-node computer cluster (each node: 2.4 GHz AMD Opteron) using a parallelized implementation in MATLAB (MathWorks), which provided a 25-fold speed-up (compared to a single-core processor) resulting in a total reconstruction time of ≈ 130 seconds. Further hardware/software-based speedup (≈ 10 -fold) is feasible.

4. Results

Simulation studies for the PARADISE method have been previously conducted (38). Here, we present and compare the results for the imaging experiments described above.

Panel (a) of Fig. 8 shows the full FOV end-diastolic (ED) image frame reconstructed from the gated CINE data. It highlights a region of interest (ROI) that includes important features

within the heart. The other panels in Fig. 8 show the ED and end-systolic (ES) reconstructed frames that are zoomed-in to the ROI for gated CINE, non-gated TSENSE rate 2 ($R=2$), non-gated TSENSE rate 5 ($R=5$), and the non-gated PARADISE (overall acceleration: 8.6) experiments as described in the previous section. Considering the high image quality and spatio-temporal resolution of the gated CINE results (Figs. 8b and 8c), we choose the CINE images as our standard reference for validating and comparing the non-gated TSENSE and PARADISE experiments. Using gated CINE results as reference, it is seen that the PARADISE images (Figs. 8h and 8i) are visually artifact-free and have a similar SNR and contrast. On the contrary, TSENSE $R=2$ frames (Figs. 8d and 8e) show motion artifacts, especially in the form of blurring in the ES frame of Fig. 8e caused by the rapid wall thickening as highlighted by the arrow. Furthermore, the reconstructed frames for the TSENSE $R=5$ scan (Figs. 8f and 8g), which had the same receiver bandwidth and TR as the PARADISE scan, are very noisy compared to the other results.

Fig. 9 shows an ejection-phase frame zoomed-in to the LV for all four scans. Relative to the CINE image in Panel (a), the PARADISE image in Panel (b) provides a sharp delineation of the LV endocardial border and the subtle papillary structure at the ejection phase. The TSENSE $R=2$ image in Panel (c) shows significant blurring at the endocardial border, which results in inaccurate visualization of the septal wall and papillary muscles. The TSENSE $R=5$ image in Panel (d) exhibits severe g-factor noise amplification and poor image quality.

Fig. 10a specifies the location of a 1D profile along the y (PE) direction and illustrates the notion of time evolution of the 1D profile intensity, referred to here as the “y-t profile.” Panels (b) to (f) of Fig. 10 show the y-t profiles for a duration of 3 heart-beats corresponding to each of the aforementioned experiments. The y-t profile for the gated CINE shown in Fig. 10b, which is periodic (hence repeated 3 times in the figure), has a temporal resolution of 14.2 ms and is used as reference. Comparing Fig. 10c to this reference, it is clearly seen that the temporal resolution of TSENSE $R=2$ is insufficient to capture the true dynamics of the heart motion. Fig. 10d shows the same TSENSE $R=2$ result but using a view-sharing (temporal sliding-window) reconstruction with 31 frames per second. Clearly, view-sharing did not provide any improvement in S-T fidelity. The y-t profile for TSENSE $R=5$ shown in Fig. 10e has better temporal resolution, although still not matching that of the CINE, but is very noisy as expected. On the other hand, the PARADISE y-t profile in Fig. 10f shows strong agreement with the CINE profile in Fig. 10a—implying that the PARADISE cine has high S-T fidelity, high S-T resolution, and accurate wall motion representation. Two ROI ellipses are marked on all y-t profiles in Fig. 10: the first ROI (on the left) includes the rapid septal wall motion during the ejection phase; the second ROI marks the LV end-diastolic wall motion including the subtle motion attributed to atrial contraction (often called the “atrial kick”). The sharp borders of the PARADISE y-t profile and its close match to that of the gated CINE profile (especially for the marked ROIs) further indicate the high S-T fidelity of the PARADISE cine and imply that its temporal resolution is close to that of the CINE.

5. Discussions

5.1. Comparison to TSENSE

As shown in Figs. 10c, 10d, and 10e, compared to the gated CINE y-t profile in Fig. 10b, the rapid ES wall thickening is not accurately captured by the TSENSE results—although TSENSE $R=5$ is better than $R=2$. For the second marked region during diastole, both TSENSE results fall significantly short. This is expected since TSENSE essentially assumes that the heart is static during the acquisition of a single frame, i.e., $N_{PE} \times TR/R$. Hence, the temporal resolution of non-gated TSENSE is fundamentally limited by this quantity, which is equal to 277 ms for the TSENSE $R=2$ experiment and 138 ms for TSENSE $R=5$. Such

temporal resolutions are below the desirable resolution of 40–50 ms typically required to provide accurate assessment of LV function for resting HRs (17, 18).

The maximum temporal frequency that can be reproduced without aliasing by real-time imaging techniques such as TSENSE (with frame-by-frame reconstruction) is given by half of its frame rate⁴, which is 1.80 Hz for the TSENSE R=2 experiment and 3.63 Hz for TSENSE R=5 (11). In the case of PARADISE, this quantity is given by $f_{\max} = 5f_{\text{avg}} + \Delta f/2 = (5+1/6)f_{\text{avg}} \approx 5.58\text{Hz}$ (Section 3.3). This analysis provides a simplified metric for the higher temporal fidelity of PARADISE evident in Fig. 10, as compared to either of the TSENSE results. Another effect of low S-T fidelity in TSENSE is demonstrated in Fig. 9c, where severe blurring of the myocardial border into the LV blood pool could result in inaccurate quantification of cardiac function. Higher temporal resolution is achievable in TSENSE by reducing the spatial resolution. However, lower spatial resolutions may lead to misestimation of the ED wall thickness due to inadequate visualization of the endocardium and papillary muscles (49).

Furthermore, the TSENSE R=5 result suffers from poor SNR. The SNR for PARADISE is far superior. More generally, the SNR penalty due to acceleration is much smaller in PARADISE than in TSENSE. The reason is two-fold: (i) in PARADISE the signal outside the adaptive- y - f support is discarded as noise; therefore, reducing input noise power; and (ii) more importantly, the overlap patterns are optimized so that the “diversity” of sensitivity-encoding is maximized (equivalently, g -factor is minimized) for each set of overlapping points in the y - f space.

Overall, as evident from Figs. 8–10, without any gating, the PARADISE method’s high acceleration and realistic (time-sequential) sampling scheme allow to match the high spatial and temporal resolutions of the parallel-imaging-accelerated gated CINE.

5.2. Relation to k-t SENSE

A comprehensive comparison of PARADISE and k-t SENSE is outside the scope of this work. Nonetheless, there are some similarities and key differences between the two methods. In particular, k-t SENSE uses a training stage to estimate the signal energy distribution in the y - f space, which is specific to the TVI being imaged. Therefore, PARADISE and k-t SENSE both utilize prior knowledge that is adapted to the cardiac dynamics of the patient; and both aim to reconstruct the TVI by recovering its representation in the y - f space. However, in k-t SENSE, utilization of the modeled S-T correlations is limited to the reconstruction procedure, whereas PARADISE also adapts the k - t acquisition based on the support model. In addition, the prior knowledge for PARADISE is a simple support model characterized by only 6 scalar parameters (Fig. 7), unlike k-t SENSE that uses the prior knowledge of a 2D signal, i.e., the y - f space signal covariance estimates (12). Finally, unlike k-t SENSE, the presented reconstruction scheme does not use a regularized matrix inversion (for Eq. [4]). Therefore, none of the issues involving regularization (13) exist for the proposed scheme.

Optimization of the k - t sampling pattern has been previously proposed for k-t BLAST/SENSE (50). The goal of that optimization was to minimize residual aliasing in the reconstructed cine. The approach in PARADISE is fundamentally different: (i) the k - t sampling pattern is designed to guarantee perfect unmixing of the y - f -space signal (for points within the estimated adaptive- y - f support); (ii) the remaining degrees of freedom in k - t space are utilized to minimize the effects of measurement noise (g -factor).

⁴Equal to half of the temporal sampling rate. Note that although view-sharing would increase the apparent frame rate, it would not affect this quantity (as demonstrated visually in Fig. 10d).

5.3. Relation to PARADIGM

A precursor of the proposed imaging method is the method of PARADIGM (34–36). The two methods share important features, specifically the time-sequential perspective on k - t acquisition, the adaptive- y - f support model, and adaptivity of both acquisition and reconstruction. However, PARADIGM is *specifically designed* for single-channel acquisition, thereby its acceleration is limited to that gained from the support model. In fact, it gains no acceleration from parallel imaging; and its reconstruction procedure is a simple filtering operation (36). It is important to note that simply undersampling the PARADIGM sampling schedule would typically result in exceedingly high g -factors and, consequently, images of little diagnostic value (38,45). Essentially, the additional acceleration provided by the double acceleration feature of PARADISE requires some *fundamental rethinking* of the PARADIGM single-channel imaging methodology. In particular, the adaptation scheme in PARADISE k - t acquisition is geared toward minimizing the SNR penalty (g -factor) that accompanies the acceleration gained from parallel imaging; and its reconstruction scheme (Section 3.2) accounts for the features of the underlying inverse problem (Section 2.3), which are structurally different from those associated with the PARADIGM method (36).

5.4. Features and Limitations

In contrast to most k - t imaging schemes, PARADISE simultaneously aims to: (i) eliminate aliasing distortion; and (ii) maximize the reconstruction SNR. This is done using a *doubly adaptive* framework: both acquisition and reconstruction are adapted to the specifics of the TVI and the desired image resolution and quality. Consequently, the PARADISE-designed acquisition (pulse sequence) varies based on the subject's physiological state, slice geometry, and resolution requirements (Fig. 7). The prescribed acquisition (Section 3.1) corresponds to an optimized y - f -space overlap pattern (with a particular form of aliasing, viz., ECs described in Section 2.3) that enables perfect unmixing of the signal (inside the y - f support) with a desirable g -factor.

The non-gated nature of the PARADISE scheme allows for capturing non-periodic motion such as the beat-to-beat motion variation in cardiac function, which potentially may contain diagnostically useful information (7); and respiratory drift. Note that capturing the respiratory drift may have significant implications for the S-T fidelity of the imaged wall motions. Moreover, we have recently demonstrated the feasibility of shallow-breathing CMRI using PARADISE (51).

Acquisition schemes that ignore the inherent MR time-sequential sampling constraint (Fig. 2) have high S-T fidelity only if the TVI has no detectable motion during acquisition time of one frame. Consequently, S-T fidelity of real-time imaging methods that ignore the time-sequential constraint is fundamentally limited by the time span of each reconstructed frame, which can be in the order of 100 ms or longer for high spatial resolutions (Section 4). Such fidelity limitations are potentially significant for several imaging scenarios including accurate wall-motion imaging (52) and visualization of fine structures such as the trabecular-papillary muscle complex (49) (for accurate function assessment) or fast moving features such as valve cusps. Instead of assuming that a plurality of PEs can be acquired instantly, the MR data acquisition and reconstruction in PARADISE explicitly account for the inherent time-sequential constraint and hence are more accurate, thereby allowing for higher S-T fidelity.

The PARADISE method is *doubly accelerated*: it gains acceleration from both the sparse adaptive- y - f support model and from parallel imaging. In general, the overall PARADISE acceleration (k - t under-sampling factor) can be decomposed into the product of two factors: *model-based acceleration*; and a *parallel-imaging acceleration*. The model-based

acceleration is inherently limited by the degree of sparsity of the adaptive- y - f support—related to the spatio-temporal correlations present in the TVI—which increases with increasing area of gaps between the model-bands and ratio of FOV_y to the dFOV size (36). Higher parallel-imaging acceleration for PARADISE comes at the price of reconstruction-noise amplification due to the underlying g -factor in the PARADISE equation (Eq. [4]) (39). However, the PARADISE method effectively utilizes additional degrees of freedom in its k - t acquisition scheme to minimize the g -factor.

Performance of all model-based techniques (including UNFOLD and k - t SENSE) in terms of the associated image quality and S-T fidelity, is limited by the accuracy of the underlying model in relation to the true object dynamics. In the proposed method, this is determined by the estimation accuracy of the adaptive- y - f support model parameters. Model mismatch, e.g., a wrong HR estimate or underestimated HR variability, may result, in some situations, in significant signal energy outside the support model. This out-of-support signal content will not be accounted for by the imaging scheme, resulting in aliasing distortion and hence loss of S-T fidelity (36,43).

6. Conclusions

This paper presents the first state-of-the-art implementation of PARADISE for functional cardiac imaging without explicit cardiac synchronization. The main advantage of the proposed doubly-adaptive approach is that by adapting and optimizing the k - t acquisition both aliasing distortion and g -factor SNR penalty are simultaneously minimized, thereby ensuring high image quality in the reconstructed cine. Consequently, compared to non-adaptive approaches, we can achieve improved spatio-temporal resolution and fidelity. As the results demonstrate, the non-gated doubly accelerated technique achieves high overall accelerations, which enable matching the high spatio-temporal resolution of parallel-imaging-accelerated gated CINE. The SNR penalty for PARADISE is far smaller than that of parallel imaging alone for equivalent accelerations. In contrast to the previously proposed k - t -based techniques, the underlying spatio-temporal support model is physiologically-driven and subject-specific. In conclusion, the in-vivo results demonstrate the feasibility of PARADISE—and its distinctive features and effectiveness—for high resolution non-gated cardiac MRI during a short breath-hold.

Acknowledgments

We acknowledge Dr. Robert J. Lederman and Ms. Annette M. Stine of the Translational Medicine Branch (TMB), NHLBI, National Institutes of Health (NIH), for supporting the imaging experiments. We thank Dr. Ashvin K. George (TMB, NHLBI, NIH) for assisting with the experiments, and Dr. Peter Kellman (Laboratory of Cardiac Energetics, NHLBI, NIH) for helping with the coil profile estimation technique. We also acknowledge Mr. Nitin Aggarwal (Univ. of Illinois) for insightful discussions. This work was partially supported by NSF grant BES 02-01876, and Ph.D. fellowships from the Beckman Institute and the Computational Science & Engineering Program, University of Illinois. The imaging experiments were partially supported by the TMB, NHLBI, National Institutes of Health.

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Figure 1. Schematic diagram describing the proposed imaging scheme and its features.

Figure 2.

Panels (a–c): Different k - t sampling schemes: (a) Non time-sequential; (b) Conventional time-sequential; (c) Lattice time-sequential. (d) Conventional time-sequential sampling: spacing of the acquired phase-encodes is dictated by the spatial Nyquist criterion and acceleration factor; and the ordering is standard (progressive). (e) Generalized time-sequential k - t lattice sampling: both the spacing and ordering of phase-encodes are controlled by the lattice parameters.

Figure 3. Localization of the dynamic FOV within the imaged slice; The bright-colored bands correspond to the model-bands located at harmonics of the average HR; For clarity, model-bands for the first harmonic and the DC band are not shown; The 1D plot on the right-hand side depicts the 1D energy spectrum corresponding to spectral analysis of the NCAT phantom (41,42); The DC component, much stronger than the harmonics, is clipped; Arrows establish the correspondence of model-band locations to the spectral energy plot.

Figure 4.

(a) Projection of the adaptive-x-y-f support model $\mathbb{B}$ onto the y - f plane produces the adaptive-y-f support in y - f space, denoted by $\mathbb{B}$, which is parameterized as shown in the figure; (b) Equivalent y - f support for the UNFOLD scheme (26), which mainly differentiates the $d\text{FOV}$ by its higher temporal bandwidth. Compared to the UNFOLD support, the structure of the adaptive-y-f support for PARADISE is sparser: for the same TVI, the area associated with the support for (a) can be smaller than (b). Further, unlike UNFOLD, which uses a single fixed support, the geometry and dimensions of the adaptive-y-f support in (a) are physiologically-driven and subject-specific.

Figure 5.

(a) Aliasing of the adaptive- y - f support B on the PSF lattice Λ^* in the y - f space; The main replica of B centered at the origin overlaps with another replica shifted to a grid point of the lattice denoted by $\Lambda^*(n_1, n_2)$ and located at $A^*\vec{n}$. Panels (b) and (c) provide a graphical construction for the equivalence class (EC) corresponding to a point (y_0, f_0) located at: (b) the origin, i.e., center of the DC band; and (c) the corner of the first model-band. In each panel, the lattice is depicted as dots. The EC in each panel (marked by circles) is constructed by centering the PSF lattice at (y_0, f_0) and finding the lattice points that lie in the support B .

Step 1. Transform the multi-channel MR data to the hybrid x - k_y - t space:

$$\text{L-channel data } \{D_\ell(k_x, k_y, t)\}_{\ell=1}^L \xrightarrow{\text{Inverse DFT along } k_x} \{D_\ell(x, k_y, t)\}_{\ell=1}^L$$

Step 2. For each $x_0 \in \text{FOV}_x$, do the following:

Figure 6.

Flowchart for the PARADISE reconstruction algorithm. First, the acquired L -channel data sampled according to the time-sequential k - t lattice Λ , denoted by $\{D_\ell(k_x, k_y, t)\}_{\ell=1}^L$, is transformed by an inverse discrete Fourier transform (IDFT) along k_x . Next, for each $x_0 \in \text{FOV}_x$, the 2D matrix $D_\ell(x_0, k_y, t)$ is zero padded to be of size $N_T \times N_{PE}$ according to Λ so that the m -th row ($m=1, \dots, N_T$) has only 1 non-zero element corresponding to the sample at $t = m\text{TR}$. The data is then transformed to the y - f space and unmixing is achieved by solving Eq. [4] for all ECs (37,38). Finally, the TVI (cine) is reconstructed by computing an IDFT along f and aggregating the results for all x_0 .

Figure 8.

Results for all four imaging experiments, zoomed-in to the region-of-interest shown in Panel (a). End-diastolic frames are shown in the top row and end-systolic frames in the bottom row. Note that the four imaging experiments correspond to different breath-holds with nonnegligible subject motion in between scans. Panels (b), (c): Gated CINE with 256×224 image matrix; Panels (d), (e): Non-gated TSENSE with rate $R=2$ acceleration and 192×192 image matrix; arrow highlights the blurring artifact; Panels (f), (g): Non-gated TSENSE with rate $R=5$ acceleration and 256×223 image matrix; Panels (h), (i): Non-gated PARADISE with 256×220 image matrix.

Figure 9.

Zoomed-in LV for an ejection-phase frame for (a) Gated CINE; (b) PARADISE; (c) TSENSE R=2; (d) TSENSE R=5. Comparing panels (a) and (b), it is seen that the PARADISE image provides a sharp delineation of the endocardial border and the subtle LV papillary structure at the ejection phase. In Panel (c), notice the blurring at the endocardial border, which results in inaccurate visualization of the septal wall and papillary muscles for the TSENSE R=2 image. In Panel (d), the severe g-factor noise amplification results in poor image quality for the TSENSE R=5 image.

Figure 10.

(a) Gated CINE frame showing the location of a 1D spatial cut along y and describing the notion of "y-t profile" as the temporal profile of the 1D cut. Panels (b) to (f) show the y-t profiles during 3 heart-beats for: (b) gated CINE; (c) TSENSE R=2; (d) TSENSE R=2 with view-sharing (temporal sliding window); (e) TSENSE R=5; and (f) PARADISE. The two marked regions-of-interest in each of the panels (b)-(f) correspond to the septal wall motion during different cardiac phases.