FULL PAPER

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Localized Spatio-Temporal Constraints for Accelerated CMR Perfusion

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Purpose: To develop and evaluate an image reconstruction technique for cardiac MRI (CMR) perfusion that uses localized spatio-temporal constraints.

Methods: CMR perfusion plays an important role in detecting myocardial ischemia in patients with coronary artery disease. Breath-hold k-t–based image acceleration techniques are typically used in CMR perfusion for superior spatial/temporal resolution and improved coverage. In this study, we propose a novel compressed sensing-based image reconstruction technique for CMR perfusion, with applicability to free-breathing examinations. This technique uses local spatio-temporal constraints by regularizing image patches across a small number of dynamics. The technique was compared with conventional dynamic-by-dynamic reconstruction, and sparsity regularization using a temporal principal-component (pc) basis, as well as zero-filled data in multislice two-dimensional (2D) and three-dimensional (3D) CMR perfusion. Qualitative image scores were used (1 = poor, 4 = excellent) to evaluate the technique in 3D perfusion in 10 patients and five healthy subjects. On four healthy subjects, the proposed technique was also compared with a breath-hold multislice 2D acquisition with parallel imaging in terms of signal intensity curves.

Results: The proposed technique produced images that were superior in terms of spatial and temporal blurring compared with the other techniques, even in free-breathing datasets. The image scores indicated a significant improvement compared with other techniques in 3D perfusion (x-pc regularization, 2.8 ± 0.5 versus 2.3 ± 0.5; dynamic-by-dynamic, 1.7 ± 0.5; zero-filled, 1.1 ± 0.2). Signal intensity curves indicate similar dynamics of uptake between the proposed method with 3D acquisition and the breath-hold multislice 2D acquisition with parallel imaging.

Conclusion: The proposed reconstruction uses sparsity regularization based on localized information in both spatial and temporal domains for highly accelerated CMR perfusion with potential use in free-breathing 3D acquisitions. **Magn Reson Med 000:000–000, 2013. © 2013 Wiley Periodicals, Inc.**

Key words: cardiac perfusion; free-breathing; compressed sensing

INTRODUCTION

Cardiac MRI (CMR) perfusion enables detection of myocardial ischemia in patients with suspected coronary artery disease (CAD) by providing an assessment of regional myocardial blood flow (1–3). Clinically, two-dimensional (2D) multislice saturation-prepared imaging is often used for evaluation of left ventricular (LV) perfusion with two to four short-axis slices acquired every R-R interval (4). Parallel imaging techniques (5–7) have been used to improve the coverage, spatial resolution, and/or temporal resolution in these acquisitions.

To improve the spatio-temporal resolution and coverage further, k-t–based acceleration techniques, such as k-t sensitivity encoding (SENSE) (8) and k-t principal component analysis (PCA) (9), which use correlations across the temporal dimension, have been applied to perfusion CMR. These techniques use a uniform undersampling of the k-space, which varies across different dynamics, resulting in a point-spread-function with lattice structure that leads to a periodic replication of the underlying image (8). The reconstruction then unfolds the resulting overlap of the image in the *x-f* domain (Fourier transform of images along the time direction) using adaptive temporal filtering, with signal correlation information derived from low-resolution training data, as well as multicoil information (9). For perfusion imaging, the central part of k-space is fully sampled in each dynamic to generate the training data. These techniques were used to acquire multislice 2D images with five-fold acceleration and 1.4 × 1.4 mm^2 in-plane resolution, with four slices acquired over two R-R intervals (10). Compressed sensing (CS), which uses the compressibility of images in a transform domain for reconstruction from incoherently undersampled data (achieved by random undersampling for Cartesian acquisition) has also been applied to perfusion CMR (11). By employing a B_1-weighted approach using multicoil information and sparsity in the *x-f* domain, up to eight-fold acceleration was achieved for the acquisition of 10 slices covering the LV (11). Other advanced reconstruction techniques based on a combination of low-rank regularization and total variation (TV) norm regularization (12), as well as group sparsity (13) have also been used in this context.

Although the aforementioned k-t–based techniques can be used for high acceleration rates, the use of temporal correlations require that the subsequent dynamics be spatially aligned. This necessitates a prolonged breath-hold acquisition, which may be difficult for many patients. Translational respiratory motion correction based on an initial reconstruction and generated by *x-f*

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space regularization has been proposed as a way of facilitating free-breathing 2D perfusion acquisitions (14). However, the reliance on an initial estimate generated by *x-f* space regularization may reduce the applicability of this technique to highly accelerated acquisitions, especially in patients with irregular breathing patterns. Rank-based regularization has also been used in acquisitions with breath-holding at the time of injection and free-breathing in later dynamics (12).

Larger coverage of the LV is necessary to fully evaluate the extent of ischemia, which is a strong predictor of outcome (15). Three-dimensional (3D) CMR perfusion has been proposed for its superior contiguous coverage and higher signal-to-noise ratio (SNR) to potentially improve the estimation of the extent of hypoperfused tissue (16,17). The contiguous coverage reduces slice misregistration errors compared with 2D imaging, facilitating accurate quantification. However, for adequate spatio-temporal resolution in 3D perfusion CMR, accelerated imaging is required. Due to the enhanced SNR, parallel imaging techniques that are commonly used for 2D multislice imaging can be applied with higher acceleration factors. Kellman et al. (16) used a six-fold acceleration factor with adaptive sensitivity encoding (6,18) in which time-varying coil sensitivity maps are generated using sliding-window reconstructions to achieve a spatial resolution of $2.3 \times 3.6 \times 10$ mm^3 with a 312-ms acquisition window on a 1.5T scanner. Shin et al. (17) used an acceleration factor of six with 2D sensitivity encoding (19) and adaptive sensitivity encoding (18) to achieve a spatial resolution of $3.0 \times 4.3 \times 10$ mm^3 in a 304-ms acquisition window at 3T. However, it was noted that such resolution may be insufficient for visualizing subendocardial defects.

To further improve the spatio-temporal resolution, k-t–based acceleration techniques have been applied to 3D perfusion. Vitanis et al. (20) reported that an improved k-t principal PCA reconstruction technique enabled 3D perfusion acquisitions with a spatial resolution of $2.3 \times 2.3 \times 10$ mm^3 in a 225-ms acquisition window at 3T. The improved reconstruction accuracy was due to the use of a compartment-based approach in which different spatio-temporal basis functions were derived for distinct spatial compartments of the heart. A combination of k-t SENSE (8) reconstruction and dual-density stack-of-spirals acquisition was used to achieve $2.4 \times 2.4 \times 9$ mm^3 spatial resolution and 230-ms temporal resolution (21) at 1.5T. B_1-weighted CS with *x-f* domain sparsity has also been reported in a feasibility study for 3D perfusion CMR (22). All of these k-t–based approaches for 3D perfusion CMR have been implemented for breath-hold acquisitions.

In this study, we sought to develop and evaluate a novel CS-based image reconstruction technique for accelerated perfusion CMR with randomly undersampled acquisitions, with applicability to free-breathing examinations. Our reconstruction relies on recently described approaches to accelerated MRI reconstruction, which demonstrate that the use of localized image features, such as compartments across temporal dynamics (20) or image patches across different parts of the volume (23), improves reconstruction quality. We hypothesized that 2D image patches in the imaging volume are varying gradually across a small number of consecutive heartbeats, even for free-breathing acquisitions, instead of the whole volume varying gradually across all dynamics as in traditional k-t techniques. We used these local spatio-temporal correlations to generate distinct sparsifying bases for different parts of the image volume. This sparsity is then used to regularize a B_1-weighted least squares problem. The performance of the proposed technique was first established with free-breathing multislice 2D acquisitions. The technique was evaluated in a number of subsequent patients, both with breath-hold and free-breathing 3D acquisitions.

METHODS

Proposed Reconstruction Technique

Randomly undersampled data with incoherent aliasing artifacts can be reconstructed using CS techniques. CS reconstruction solves a regularized least-squares problem, enforcing data consistency with the measured k-space locations, also allowing for the incorporation of coil sensitivities in a B_1-weighted approach, and using a sparsifying transform for exploiting the compressibility of the image volume. For perfusion, conventional CS algorithms use the *x-f* space or the *x-pc* space for sparsification in which the principal components (pc) are derived for the whole volume.

The proposed reconstruction approach uses distinct spatio-temporal sparsifying functions based on PCA for different parts of the imaging volume to compensate for various physiological changes. The use of a distinct pc basis for different parts of the imaging volume is depicted in Figure 1. In perfusion imaging, different anatomies exhibit different contrast uptake, resulting in distinct temporal correlations. In compartment-based k-t PCA, this was exploited by defining compartments of interest for the right ventricle (RV), LV, myocardium, and others. In the proposed algorithm, we extend the use of compartments to $N_b \times N_b$ 2D image patches. This allows us to consider overlapping image patches within the same slice, leading to an overcomplete representation, which was shown to improve reconstruction quality in CS (23). It further facilitates the use of this technique with free-breathing data, since the correct determination of individual compartments for distinct structures such as RV, LV, or myocardium as described by Vitanis et al. (20) requires the alignment of different dynamics. The second component of the proposed approach is that only N_{dyn}-consequent dynamics are considered when generating the sparsifying transforms, instead of all of the dynamics, as in traditional k-t methods. This is based on the hypothesis that even with moderate free-breathing, the displacement over a small number of consecutive heartbeats will be regular and not severe. Consequent dynamics is used in an overlapping fashion to lead to an overcomplete representation.

The algorithm was implemented in two stages using a bootstrap method (24) in which an initial reconstruction is used to generate the distinct principal components for each $N_b \times N_b \times 1 \times N_{dyn}$ overlapping image volumes, as in Figure 1. These bases are subsequently used to

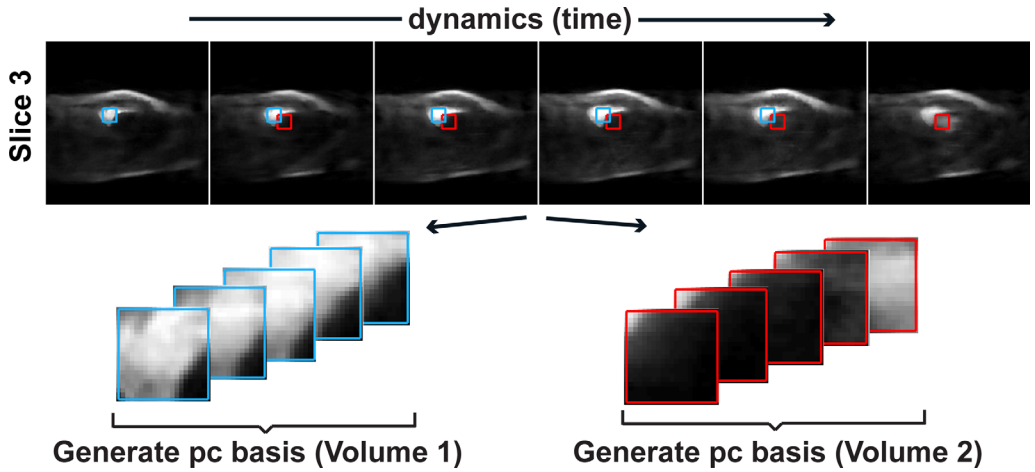

FIG. 1. Process of generating the distinct temporal pc basis for each 10 × 10 × 1 × 5 volume (in *x-y-z-t* space). An initial dynamic-by-dynamic TV-regularized estimate was used to localize each such overlapping volume (e.g., those with blue or red patches). The patches were combined together into a 100 × 5 matrix, and the right singular vectors were used as the temporal pc basis for that volume in the proposed reconstruction. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

sparsify the overlapping image volumes for regularization in the second and final stage of the reconstruction.

Both stages of reconstruction rely on a B_1-weighted approach in which the coil sensitivity information is used for data consistency during the reconstruction (11,25). Based on iterative soft thresholding (26), every iteration of the B_1-weighted algorithm can be summarized as follows:

1. the current combined-coil image estimate is denoised using the regularization function (e.g., TV regularization);
2. the combined image is mapped to individual coils via voxel-wise multiplication with the sensitivity map of that coil;
3. data consistency with the measured data is enforced by Fourier transforming the coil images, replacing the acquired k-space locations with the acquired lines, and inverse Fourier transforming to acquire data-consistent images; and
4. the data-consistent coil images are combined using the coil sensitivity maps, where the voxel-wise product of the coil images and conjugate of the coil sensitivity maps were summed across the coil dimension, to generate the next image estimate.

Normalized relative coil sensitivity maps were generated for each dynamic by Hanning filtering the fully sampled central k-space of each dynamic in the k_y-k_z direction, inverse Fourier transforming these filtered k-space data to get a low-resolution image for each coil, and normalizing each coil image by the root-sum-squares combination of all coil images.

For the first stage of the algorithm, a basic estimate of the images was generated, which was then used to derive distinct pc bases for each $N_b \times N_b \times 1 \times N_{dyn}$ overlapping image volumes. For the proposed implementation, N_b was chosen to be 10, and N_{dyn} was set to 5. Two types of basic estimates were compared visually in a pilot study: 1) A CS reconstruction with spatial TV regularization (with TV term weight = $\times 10^{-4}$ the maximum absolute voxel intensity value of the zero-filled data) for reconstructing each dynamic individually and 2) a low-resolution image generated from the fully sampled central k-space lines. Subsequently, the preferred way of generating the basic estimate was used for all the proposed reconstructions.

In the second stage, these distinct pc bases were used for regularization in the B_1-weighted algorithm (with the regularization term weight = 10^{-3} times the maximum absolute voxel intensity value of the zero-filled data) as described previously. Hence, the first stage of each iteration of the B_1-weighted algorithm was modified as follows: each $N_b \times N_b \times 1 \times N_{dyn}$ overlapping image volume of the current combined-coil image estimate was sparsified using the corresponding pc basis for that volume, thresholded using soft thresholding, and inverse-transformed. These overlapping thresholded volumes were combined by simple averaging to generate the thresholded estimate. The proposed reconstruction was implemented using MATLAB software (version 7.6, MathWorks, Natick, Massachusetts, USA).

In Vivo Imaging

All imaging was performed on a 1.5T Philips Achieva (Philips Healthcare, Best, The Netherlands) system with a 32-channel cardiac phased-array receiver coil and without vasodilator stress. For this HIPAA-compliant study, the imaging protocol was approved by our institutional review board. Written informed consent was obtained from all participants.

Accelerated 2D Perfusion

2D multislice perfusion images were acquired on a healthy 21-year-old female subject without contraindications to MRI. After the first few heartbeats, 0.05 mmol/kg gadobenate dimeglumine (MultiHance, Bracco, Rome, Italy) was intravenously injected with a power injector at a rate of 4 mL/s, followed by a 10-mL saline flush. An electrocardiogram-triggered, saturation recovery gradient-

echo (GRE) perfusion sequence was used for acquisition on the LV short axis with anterior–posterior phase encoding. The imaging parameters were as follows: repetition time/echo time = 3.2/1.6 ms; flip angle = 20°; spatial resolution = 1.6 × 1.6 mm^2; slice thickness = 10 mm; number of slices = 5; field-of-view = 320 × 320 mm^2; saturation prepulse delay = 100 ms. The acquisition was prospectively accelerated by a rate of 4 by keeping the central 22 k-space lines and randomly undersampling the outer k-space, resulting in an acquisition window of 155 ms per 2D slice. The acquisition was performed with free-breathing and no breath-holding instructions.

Accelerated 3D Perfusion

Ten patients (46.7 ± 14.1 years; 7 men) referred for clinical CMR and five healthy subjects (41.6 ± 26.4 years, 2 men) without contraindications to MRI were recruited for 3D rest perfusion CMR. An electrocardiogram-triggered, saturation recovery gradient-echo perfusion sequence was used for acquisition. After the first few heartbeats, 0.05 mmol/kg gadobenate dimeglumine (MultiHance) was intravenously injected with a power injector at a rate of 4 mL/s, followed by a 10-mL saline flush. A truncated RF excitation pulse (flip angle = 20°) was used for a reduced repetition time/echo time of 2.1/1.2 ms. Images were acquired in the LV short axis with foot–head phase encoding (spatial resolution = 2.3 × 2.3 × 10.0 mm^3; field of view = 340 × 340 × 80 mm^3) where the two edge slices were discarded to generate six sectional slices. A saturation prepulse delay of 100 ms was used with an acquisition time of 250 ms per heart beat. Six of the acquisitions were acquired during a breath-hold at the time of injection; the remaining acquisitions were acquired with free-breathing throughout the scan. The acquisition was performed for 30 seconds, which corresponded to an average number of dynamics of 38 ± 11 (range, 17–57). Data acquisition was prospectively accelerated by a rate of 7.5 with respect to an elliptical window (10-fold with respect to the whole k-space) in k_y-k_z using a pseudorandomly generated undersampling pattern. A central k-space of size 11 × 3 in k_y-k_z, corresponding to 3.5% of the k-space, was fully sampled, and the outer k-space was randomly undersampled. A modified radial k_y-k_z phase reordering scheme in which the centermost k-space line was allowed to be sampled first was used to mitigate flow artifacts and eddy currents by reducing gradient switching (27). Additionally, breath-hold multislice 2D perfusion was acquired in four healthy subjects (age, 46.5 ± 27.8 years; 2 men) using the same sequence parameters as the aforementioned 2D sequence, but with SENSE rate 2.7 for accelerated imaging. The order of the breath-hold multislice 2D and the 3D acquisitions were randomized, with a 40–50 minute wait between the two perfusion scans.

Image Reconstruction

The k-space data were exported and transferred to a stand-alone workstation for further analysis. The proposed reconstruction was performed off-line as described above. Comparison images were generated via three different B_1-weighted reconstructions using the same coil sensitivity maps:

1. zero-filling of the measured data, where the k-space lines that were not acquired were replaced with zero, and an inverse Fourier transform was applied for the zero-filled images;
2. each dynamic was reconstructed individually using TV regularization, referred to as dynamic-by-dynamic reconstruction; and
3. deriving a principal component basis for the whole volume from the central k-space lines as in conventional PCA-based techniques (9,24) and using this *x-pc* sparsity for regularization.

A flowchart for a single iteration of the B_1-weighted algorithms and a summary of the thresholding techniques are shown in Figure 2. For the B_1-weighted reconstructions of the 3D datasets, the data from the edge coils, where folding artifacts may occur due to the limited FOV in the foot–head phase encoding direction, were not included in the B_1-weighting. The typical reconstruction times for the MATLAB-only implementation of these techniques were: ∼20 minutes for the dynamic-by-dynamic TV reconstruction, ∼45 minutes for the x-pc regularized CS reconstruction, and ∼90 minutes for the proposed reconstruction (110 minutes including the first TV reconstruction).

Image and Statistical Analysis

A qualitative assessment of image quality was performed for all 3D reconstructions. All reconstructions were written into DICOM format and imported into ViewForum software (version R4.2V1L2, Philips Healthcare) for qualitative evaluation by two experienced blinded reviewers independently using a four-point scale system: 1, poor or uninterpretable (myocardium, RV, and LV boundaries not visible or with markedly blurred borders and edges); 2, fair (myocardium, RV, and LV visible, with moderately blurred borders and edges); 3, good (myocardium, RV, and LV visible, with mildly blurred borders and edges); 4, excellent (myocardium, RV, and LV visible, with sharply defined borders and edges). Imaging scores are presented as the mean ± one standard deviation. A signed rank test was used for imaging scores in pair-wise fashion to test for the null hypothesis that the central tendency of the difference was zero for the proposed and other reconstructions. All statistical analyses were performed using SAS software (version 9.3, SAS Institute, Cary, North Carolina, USA); $P < 0.05$ was considered significant.

For the four healthy volunteers, for which both an accelerated 3D acquisition and a breath-hold multislice 2D perfusion with parallel imaging were acquired, region-based time intensity curve analyses were performed. The analysis was performed on the mid-short-axis slice of the 3D volume and the 2D stack (21), using QMASS MR software (version 7.2, Medis, Leiden, The Netherlands). The endocardial and epicardial contours were drawn on each dynamic several pixels from the outer and inner borders to limit signal contamination. The contrast uptake curves were then generated for the

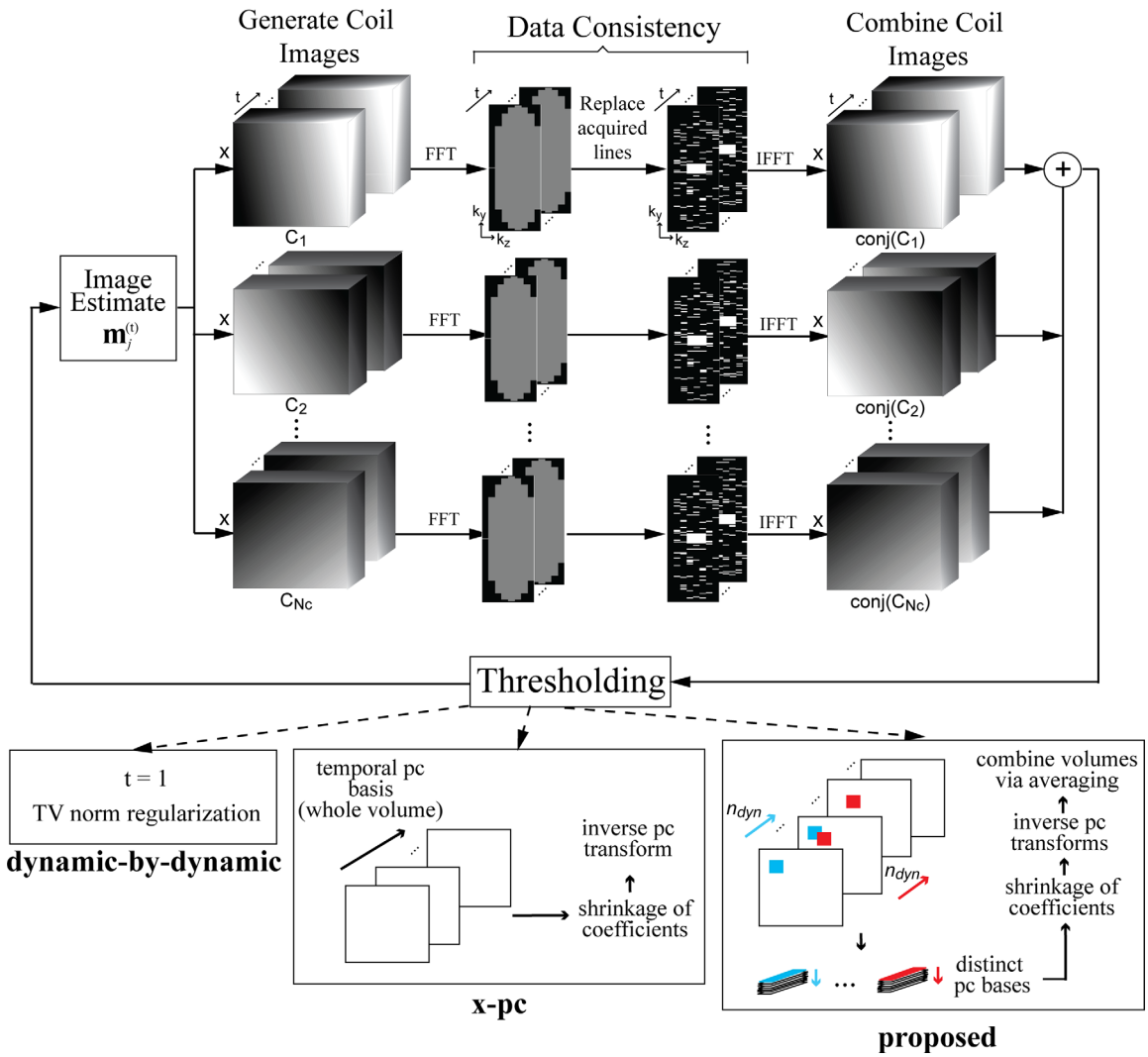

FIG. 2. Flowchart for a single iteration of the B_1-weighted algorithms used in this study. At every iteration, the current image estimate was mapped to individual coil images by voxel-wise multiplication with sensitivity maps. Data consistency was enforced by replacing the acquired k-space lines study (3D k-space is depicted here). A combined image was generated by summing the voxel-wise product of data-consistent coil images and conjugate of coil sensitivity maps across the coil dimension. This image was then thresholded using one of the three techniques described (dynamic-by-dynamic, x-pc, or the proposed regularization). (FFT = fast Fourier transform, IFFT = inverse FFT). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

LV blood pool and the myocardium for the commercially available SENSE reconstruction for the multislice 2D acquisition and the proposed reconstruction for the 3D acquisition.

RESULTS

Rest first-pass perfusion CMR was successfully completed in all subjects without complications. Figure 3 shows the results of the pilot study in a 3D dataset to determine the first-stage estimate, which would be used to generate the distinct pc bases for the proposed regularization, comparing a dynamic-by-dynamic spatial TV reconstruction with a low-resolution image generated from the central k-space. The starting images based on the two techniques are shown in Figure 3a, where significant partial voluming effects are observed for the low-resolution image. The corresponding reconstructions using the proposed regularization based on the pc bases derived from these images are shown in Figure 3b. Improvement in reconstruction quality is visualized when the pc bases are derived from the spatial TV regularized reconstruction, which is used for the first stage of the algorithm in all subsequent reconstructions.

Figure 4 shows various reconstructions of all the slices of the multislice 2D acquisition in an example dynamic after the contrast arrival in the LV. Reconstructions using the dynamic-by-dynamic TV reconstruction (second row) removes a substantial amount of the ghosting artifacts along the phase encoding direction apparent in the acquired data (first row); however, it is still blurry due to the high undersampling rate. The x-pc reconstruction (third row) and the proposed reconstruction (fourth row) both yield sharper images. The proposed reconstruction shows more signal homogeneity in the LV and RV blood pools compared with the x-pc reconstruction, potentially

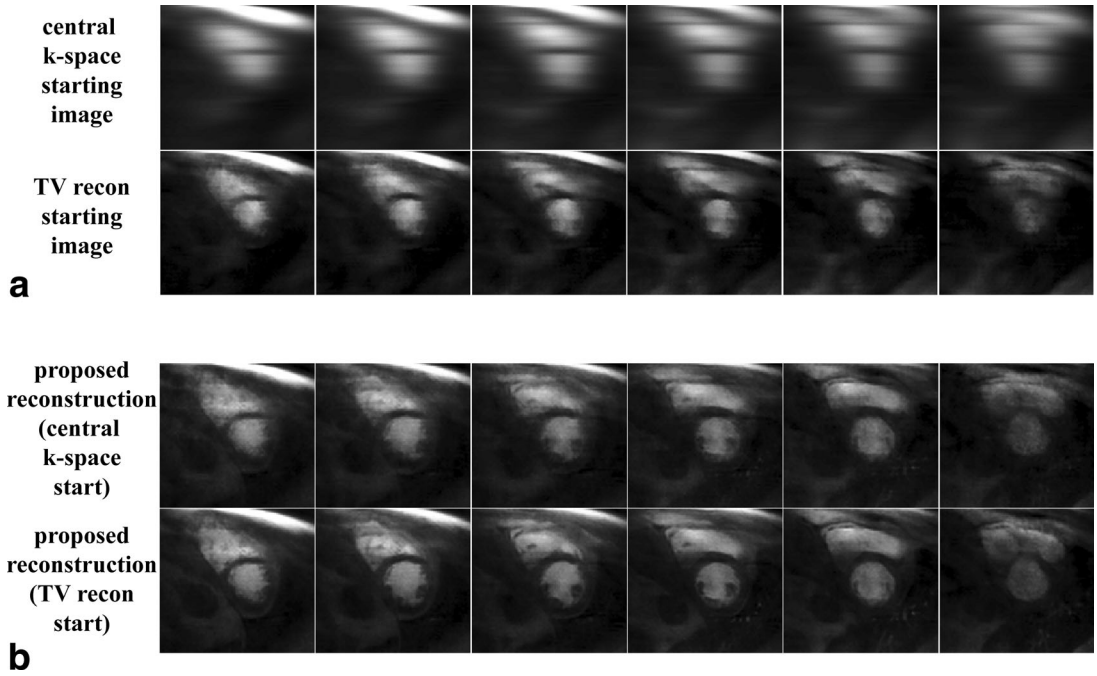

FIG. 3. Comparison of a low-resolution image from fully sampled central k-space with spatial TV-regularized reconstruction to generate the distinct pc bases for the proposed reconstruction in a 3D dataset. **a:** Low-resolution images show significant partial voluming effects due to small center size (11 $\times$ 3 in k_y-k_z) compared with TV reconstruction. **b:** The corresponding reconstructions using the proposed regularization indicate visual improvement when the TV reconstruction is used to generate distinct pc bases for each 10 $\times$ 10 $\times$ 1 $\times$ 5 volume.

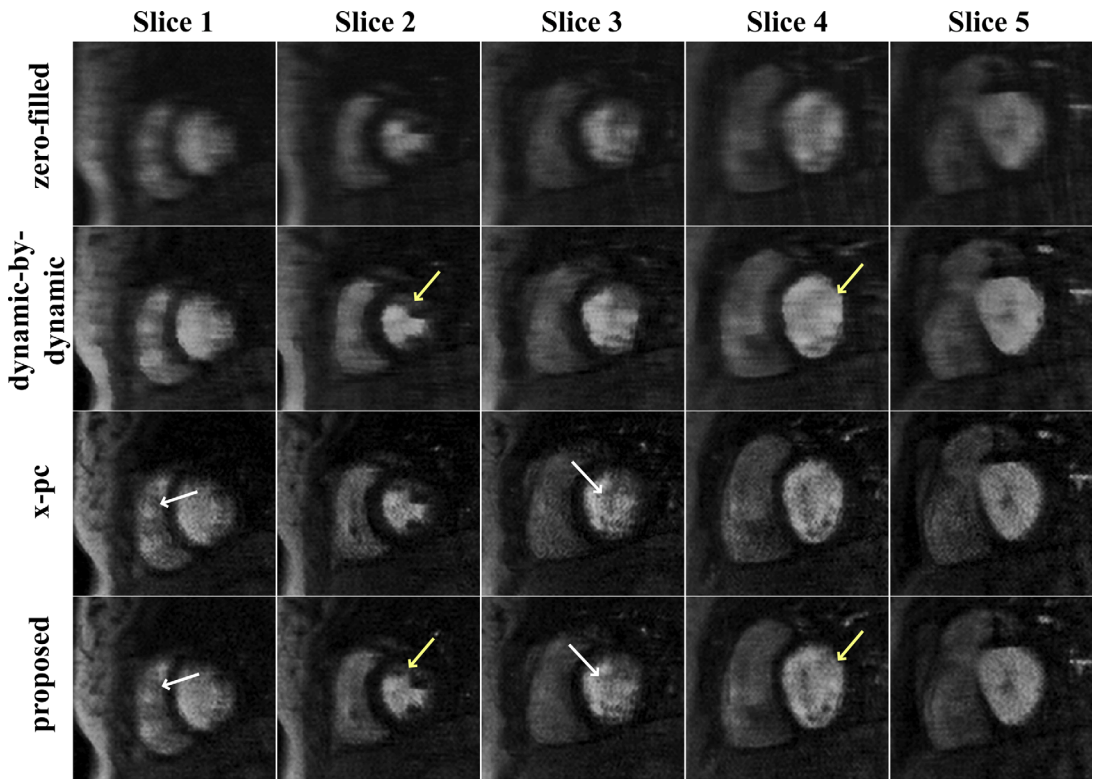

FIG. 4. All slices of the multislice 2D acquisition from a healthy subject in a dynamic after the contrast arrival in the left ventricle (LV) during free-breathing. The acquired (zero-filled) data are shown in the first row; the blurriness and aliasing artifacts are due to the rate-4 undersampling. The second row shows reconstructions using the dynamic-by-dynamic TV method, which removes a substantial amount of the ghosting artifacts but is still blurry due to the high undersampling rate (yellow arrows). The x-pc reconstruction (third row) and the proposed reconstruction (fourth row) both have sharper edges. The proposed reconstruction shows more signal homogeneity in the LV and RV blood pools compared with the x-pc reconstruction (white arrows).

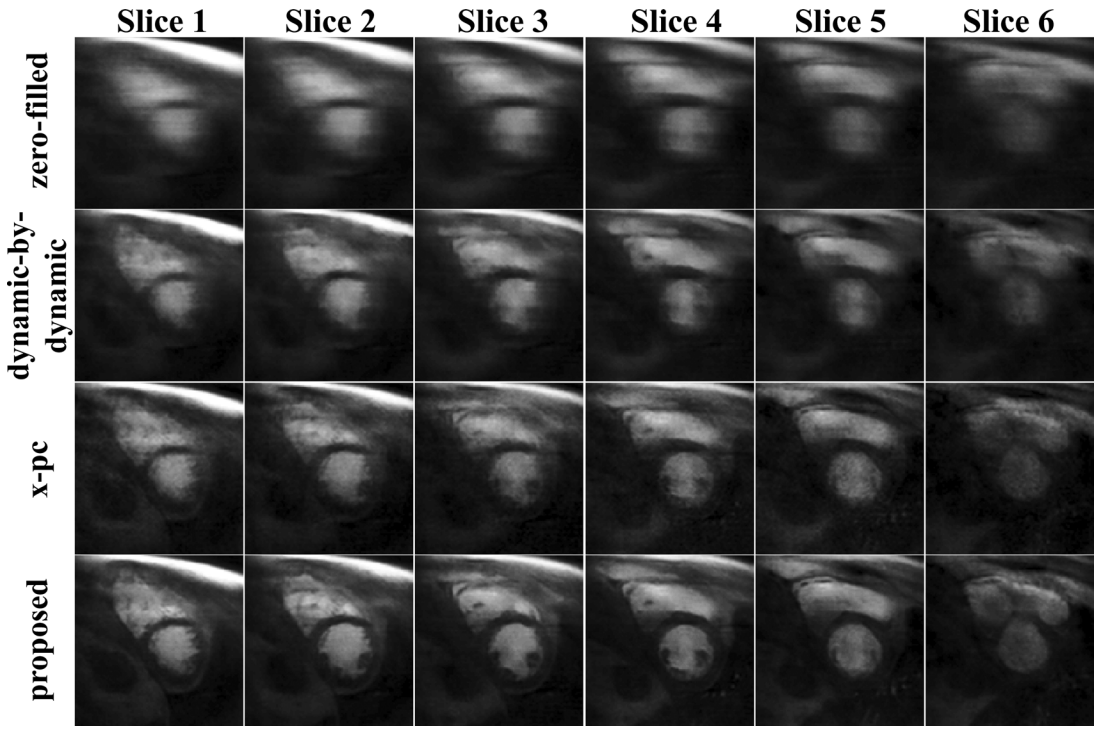

FIG. 5. Slices of a 3D dataset from a subject in a dynamic after the contrast arrival. The acquired (zero-filled) data are shown in the first row. Reconstructions using the proposed method (fourth row) have good temporal fidelity and are sharper compared with dynamic-by-dynamic CS reconstruction (second row) and x-pc CS reconstruction (third row), both of which show blurred artifacts.

due to a reduction in the reconstruction artifacts based on the regularization, in view of the free-breathing nature of the acquisition.

Figure 5 shows slices of a highly undersampled 3D acquisition from a patient in a dynamic after contrast arrival. The dataset was acquired with breath-holding at the time of injection, hence it includes both free-breathing and breath-hold dynamics. The dynamic-by-dynamic TV reconstruction has limited use in removing the aliasing, and incurs spatial blurring artifacts due to the high undersampling rate. The x-pc regularized reconstruction is sharper compared with the TV reconstruction, but there are residual artifacts due to the free-breathing dynamics. The proposed reconstruction shows good temporal fidelity with clearly defined blood–myocardium borders. Figure 6 shows slices of a 3D dataset from another subject. This dataset was also acquired with a mix of free-breathing and breath-hold dynamics, with breath-holding at the time of injection. The TV reconstruction removes some of the aliasing artifacts from the acquired image. Sharper images are obtained with the x-pc regularized reconstruction, although residual artifacts are apparent. The proposed reconstruction leads to a sharp and less noisy image compared with the other reconstructions.

Figure 7 shows dynamics of the middle slices of the 3D volume from a subject in which the acquisition was free-breathing throughout the scan. Due to the high undersampling rate, the dynamic-by-dynamic TV reconstruction suffers from spatial blurring, even though some of the aliasing artifacts have been suppressed compared with the zero-filled acquisition data. The x-pc reconstruction suffers from residual respiratory motion due to temporal blurring. The proposed method offers a clearer visualization of the LV and RV, as well as the myocardium even in the presence of respiratory motion. Overall qualitative image scores demonstrate that the proposed method (2.8 ± 0.5) is significantly better than x-pc regularized CS (2.3 ± 0.5, $P < 0.01$), dynamic-by-dynamic TV-regularized CS (1.7 ± 0.5, $P < 0.01$), and zero-filled images (1.1 ± 0.2, $P < 0.01$).

Figure 8 shows images that correspond to the peak RV, LV, and myocardial enhancement across all slices, using the 7.5-fold accelerated 3D acquisition with the proposed reconstruction (Fig. 8a), and 2.7-fold accelerated multislice breath-hold 2D acquisition using the commercially available SENSE reconstruction (Fig. 8b) in a healthy subject. The corresponding signal intensity curves indicate similar dynamics of contrast uptake both in the LV blood pool (Fig. 8c) and across the myocardium (Fig. 8d).

DISCUSSION

In this study, we proposed and evaluated a CS-based reconstruction technique for CMR perfusion that uses local information in both spatial and temporal domains, and that can be applied to highly accelerated free-breathing multislice 2D and 3D myocardial perfusion. The proposed reconstruction uses coil sensitivity information and sparsity regularization based on an overcomplete representation obtained by deriving distinct principal component bases for each $N_b \times N_b \times 1 \times N_{dyn}$ overlapping image volume in the B_1-weighted image.

The feasibility of the proposed reconstruction method was first evaluated in multislice 2D perfusion, and its efficacy was subsequently implemented in 3D perfusion.

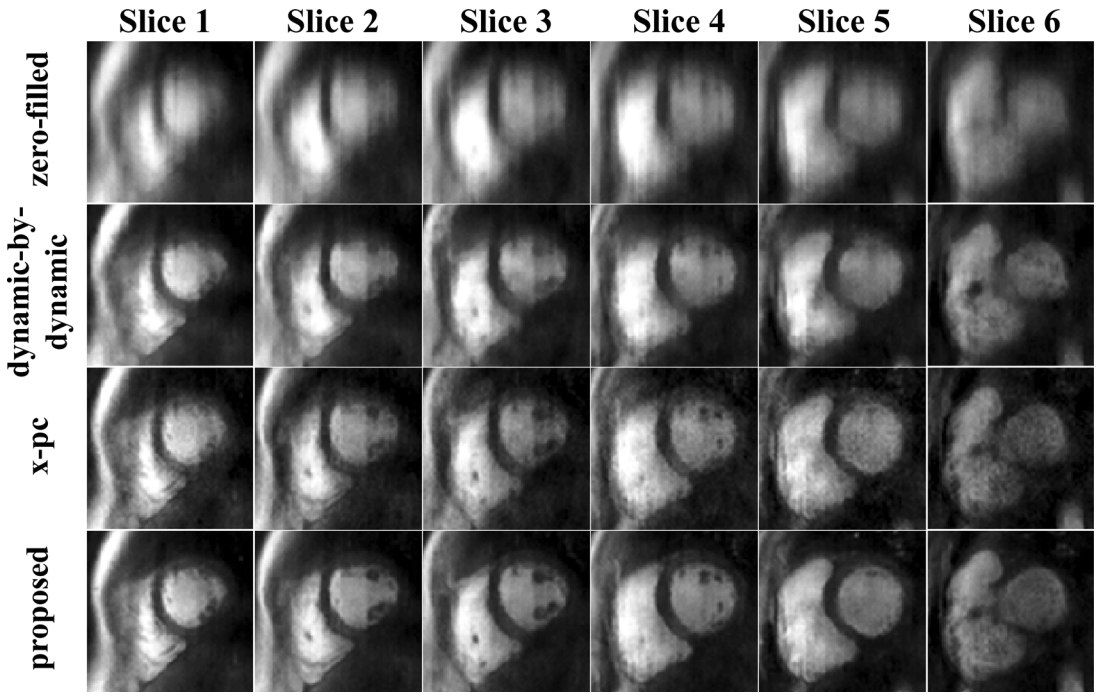

FIG. 6. Slices of a 3D dataset from a subject in a dynamic after the contrast arrival. The blood–myocardium border is more clearly visualized using the proposed method (fourth row), whereas residual aliasing artifacts are present in the other reconstructions.

The nature of these acquisitions is vastly different. In multislice 2D, a four-fold acceleration is sufficient to acquire each slice with a sufficient temporal window of ~150 ms for the given imaging parameters. For 3D imaging, however, a substantially higher acceleration rate of 7.5-fold is necessary to acquire the volume in a temporal

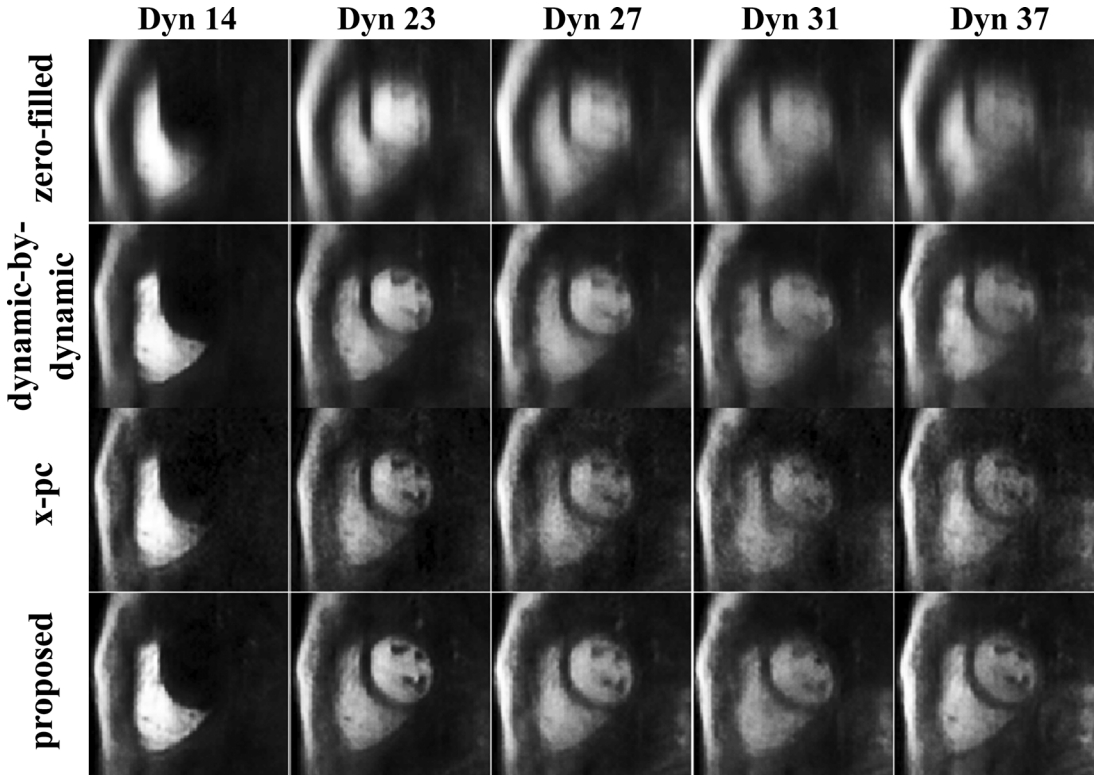

FIG. 7. Dynamics of a middle-section slice from a 3D dataset acquired in free-breathing. The LV, RV, and myocardium are delineated using the proposed method even in the presence of respiratory motion (fourth row). The x-pc reconstruction shows residual respiratory motion due to temporal blurring (third row). The dynamic-by-dynamic reconstruction shows spatial blurring due to the high undersampling rate (second row).

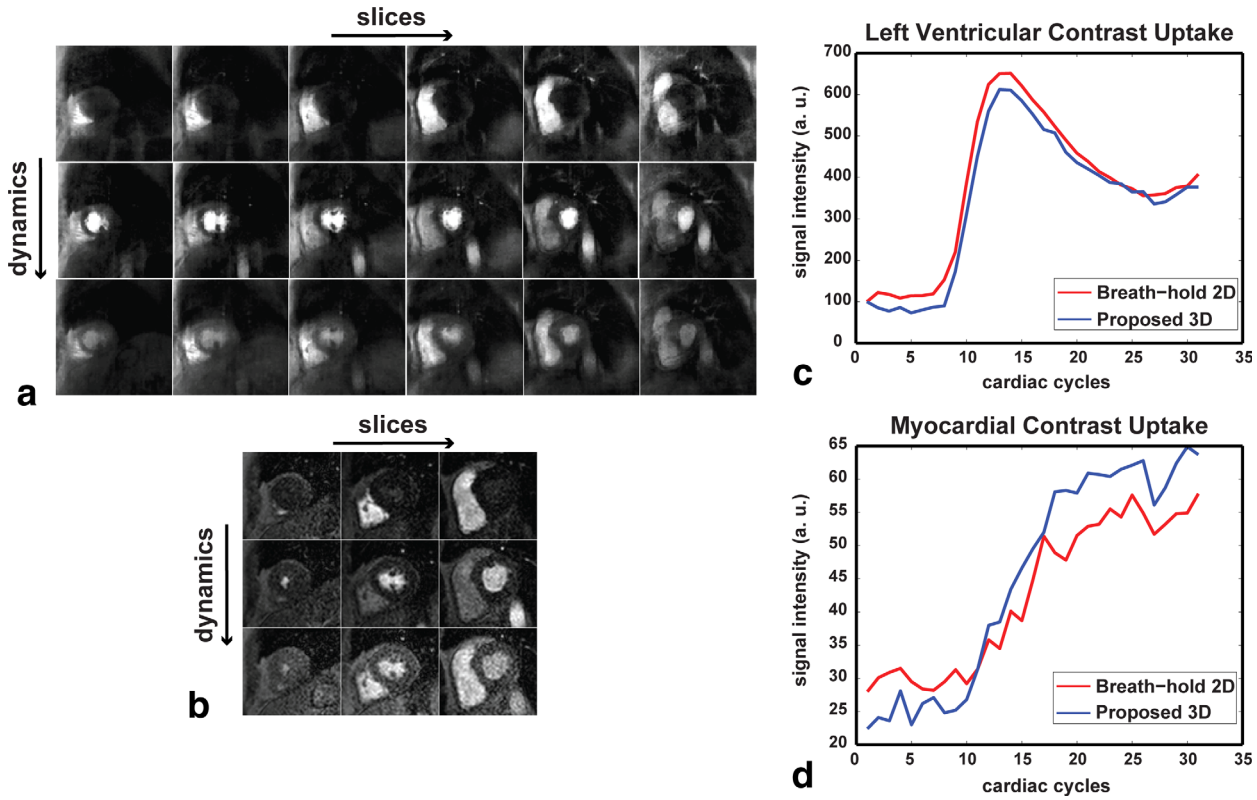

FIG. 8. Images generated using the 7.5-fold accelerated 3D acquisition with the proposed reconstruction (**a**), and 2.7-fold accelerated multislice breath-hold 2D acquisition using the commercially available SENSE reconstruction (**b**) in a healthy subject, depicting the peak RV, LV, and myocardial enhancement across all slices. The signal intensity curves show similar dynamics of contrast uptake in the LV blood pool (**c**) and the myocardium (**d**). There are differences due to the order of imaging (3D acquisition was performed first during the same examination), contrast differences between reconstructions using commercially available software, and raw data reconstruction. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

window of 250 ms. Even in the presence of higher SNR for 3D acquisitions, this higher rate may hinder the reconstruction progress. The effects of the higher acceleration rate were apparent in the reconstructions presented. Whereas in multislice 2D the difference between x-pc and the proposed reconstruction was most apparent in signal homogeneity, the difference was larger in 3D acquisitions, where the proposed method provided shaper borders, which at times were not visualized with the other reconstructions.

Previous applications of CS to randomly undersampled 3D perfusion imaging have been limited to regularization using *x-f* sparsity or spatio-temporal TV norm (22,28). For 2D datasets acquired with a combination of breath-holds and free-breathing, these regularization techniques tend to suffer from respiratory artifacts (12). In this study, by using a technique that uses localized spatio-temporal acquisition, the feasibility of randomly undersampled 3D perfusion with free-breathing acquisitions was established.

The proposed technique uses a two-step procedure of first generating a basic estimate and then using this estimate for generating the principal component bases for each localized spatio-temporal volume. The two-step procedure has been previously used in dynamic MRI, where the initial estimate has been generated using *x-f* space sparsity (14,24,29). In this study, we chose to use TV norm regularization for each dynamic individually to avoid possible temporal blurring artifacts due to the use of a spatio-temporal regularizer. The dynamic-by-dynamic TV reconstruction sufficiently suppresses ghosting artifacts related to random undersampling at the cost of spatial blurring for the acceleration rates used in this study. However, if higher acceleration rates are used, a dynamic-by-dynamic TV reconstruction may not sufficiently suppress the aliasing artifacts. An alternative is to use low-resolution images generated from the central k-space as described by Vitanis et al. (20). However, our results indicate that for the small center size used in this study for 3D datasets, these low-resolution images suffer from partial voluming artifacts and hence do not have sufficient spatial resolution to generate principal component bases of adequate quality for effective use of the spatio-temporal localization. Further studies are needed to determine the use of low-resolution images with larger central k-space sampling in determining the principal component bases for higher acceleration rates.

An alternative technique for the two-step procedure is the use of low-rank constraints for reconstruction of dynamic MRI (12,30). These techniques vectorize each time frame and arrange these time frames into a matrix, which may have low-rank properties. The rank of such a matrix is upper-bounded by the number of dynamics used in the formation of the matrix. The low-rank

assumption further assumes that there exists a matrix that closely approximates this matrix with a much smaller rank. In our case, we use matrices of 100×5, as determined by the choice of block size for the 2D patches and the temporal extent to which correlations are exploited. These matrices inherently have a rank of 5 at most, even in the presence of aliasing artifacts. Due to this low rank, the low-rank techniques were found to be not applicable to this problem in a preliminary study (data not shown). However, the rank regularization techniques have the advantage of not relying on previous estimates, as well as the use of singular vectors in both spatial and temporal directions. Hence, the use of rank regularization techniques for smaller block sizes or larger temporal windows warrant further investigation.

A possible extension to the proposed algorithm is to use different patch sizes according to the image content. For relatively uniform areas such as the blood pools, a larger patch size can be used, whereas smaller patches can be used for the myocardium. Use of shape-adaptive patches may further improve the adaptability of the algorithm (31). These approaches might be useful in reducing the reconstruction time or increasing the reconstruction quality by incorporating further prior information. However, this was not studied in the current study.

In our study, the size of the fully acquired central k-space was not systematically studied, which is especially important in accelerated 3D perfusion. In our previous experience with CS in segmented 3D acquisitions, we have developed an empirical rule-of-thumb of sampling the central k-space corresponding to ~4%–5% of the whole k-space. However, with an undersampling rate of 7.5 for the 3D acquisitions and an elliptical shutter, this would require approximately half of the acquired lines to be sampled from the center of k-space. Hence, based on our initial reconstructions, we have opted to acquire 30% of our data from the central k-space, which may be insufficient. Alternatively, an elliptical shutter might be applied to the central lines as well instead of acquiring a fully sampled rectangle. However, this approach was not implemented for this study.

For the CS reconstructions in this study, the weights of the regularization terms and thus the corresponding thresholding parameters were chosen empirically as in other CS studies (11,23,24,29). Furthermore, for the proposed algorithm, there are additional parameters, N_b and N_{dyn}, that need to be chosen *a priori*. The effects of varying this parameter were studied by varying N_b among {5, 10, 20} and N_{dyn} among {3, 5, 10} and performing the proposed reconstruction for each of these nine pairs of (N_b, N_{dyn}). Based on this study (results not shown), for small N_b or N_{dyn}, it is difficult to remove aliasing artifacts leading to blurrier images. Similarly, for large N_b or N_{dyn}, the reconstruction introduces spatial or temporal blurring, respectively, with the x-pc CS reconstruction representing the limiting case of using the whole volume. Thus, we have empirically set these parameters for an adequate trade-off between removing aliasing artifacts and avoiding spatio-temporal blurring due to signal averaging.

Our study has limitations. More spatial coverage of the LV and improved spatial resolution may be necessary for the identification of perfusion defects or to avoid dark rim artifacts (32). The temporal resolution of the 3D acquisitions may still be longer than the quiescent period of the heart, thus these acquisitions may be susceptible to cardiac motion. We have not provided comparisons against the currently used compartment-based k-t PCA reconstruction. This reconstruction is designed to work with uniform undersampling, which conflicts with the random undersampling used in this study, and hence requires an extra acquisition. We have not provided SNR measurements because CS algorithms inherently threshold the noise, making it difficult to locally characterize the noise in the reconstructions. Further clinical studies are needed to assess its diagnostic value in patients with suspected coronary artery disease, as well as in subjects with highly irregular breathing patterns or in the presence of exercise stress.

CONCLUSION

We have demonstrated a reconstruction technique that uses coil sensitivity information and sparsity regularization based on localized information in both spatial and temporal domains for highly accelerated CMR perfusion with potential use in free-breathing 3D acquisitions.

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