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Four-Dimensional Respiratory Motion-Resolved Whole-Heart Coronary MRA

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ABSTRACT

Purpose: Free-breathing whole-heart coronary MRA commonly uses navigators to gate respiratory motion, resulting in lengthy and unpredictable acquisition times. Conversely, self-navigation promises 100% scan efficiency, but requires motion correction over a broad range of respiratory displacements, which may introduce image artifacts. We propose to replace navigators and self-navigation with a respiratory motion-resolved reconstruction approach.

Methods: Using a respiratory signal extracted directly from the imaging data, individual signal-readouts are binned according to their respiratory states. The resulting series of undersampled images are reconstructed using an eXtra-Dimensional Golden-angle RAdial Sparse Parallel imaging (XD-GRASP) algorithm, which exploits sparsity along the respiratory dimension. Whole-heart coronary MRA was performed in 11 volunteers and 4 patients with the proposed methodology. Image quality was compared to that obtained with 1D respiratory self-navigation.

Results: Respiratory-resolved reconstruction effectively suppressed respiratory motion artifacts. The quality score for XD-GRASP reconstructions was greater-than or equal-to self-navigation in 80/88 coronary segments, reaching diagnostic quality in 61/88 segments vs. 41/88. Coronary sharpness and length were always superior for the respiratory-resolved datasets (e.g. sharpness mid-LAD $40.8 \pm 9.1\%$ vs $34.9 \pm 10.2\%$), reaching statistical significance ($p < 0.05$) in most cases.

Conclusion: XD-GRASP represents an attractive alternative concept for handling respiratory motion in free-breathing whole-heart MRI, and provides an effective alternative to self-navigation.

Keywords: Coronary MRA, Free Breathing, Sparse Reconstruction, Motion-Correction, Self-Navigation

INTRODUCTION

Coronary MR angiography (MRA) has improved substantially over the past two decades, showing promising results in relatively large patient cohorts (1-4). However, it still remains mostly confined to research use at a small number of experienced academic MR centers. The main shortcoming of coronary MRA is its vulnerability to motion-induced artifacts, which is linked with time-inefficient data collection. Conventional acquisitions are electrocardiogram (ECG)-triggered to short time windows (~50-100ms) of relative coronary quiescence (e.g. mid-diastole) and a large number of cardiac cycles is needed for sufficient high-resolution volumetric coverage. Consequently, free-breathing acquisitions are mandatory, but necessitate sophisticated respiratory motion compensation approaches.

Navigator techniques (5-8), which identify the position of the right hemidiaphragm, typically gate data collection to a small acceptance window in end-expiration only. The drawbacks of these techniques include low scan efficiency, unpredictable scan times, sensitivity to respiratory drift, and the need for meticulous scan planning. Conversely, self-navigated techniques (9-14) that directly extract a respiratory motion signal from the imaging data to perform respiratory motion correction, operate with 100% scan efficiency, have highly predictable scan duration, and improved ease-of-use. Such techniques have been extensively tested in both volunteer (10,15,16) and patient (14,17) cohorts in single center studies. However, self-navigation still suffers from limitations related to the motion model employed for correction (e.g. 1D, 3D, affine, etc) (18), may not be sufficiently accurate for large scale respiratory motion, and may be affected by artifacts originating from static anatomy after motion correction.

Several 3D self-navigation approaches have recently been proposed to subdivide the whole-heart coronary dataset into subsets of volumes, each corresponding to a particular respiratory position or state (12,13,19,20). As the quality of these imaging volumes is generally low due to the inevitable undersampling artifacts, all such methods propose to exploit these subsets uniquely for image registration, while the final reconstructed dataset is composed of all acquired k-space lines after motion correction. In this context, it has to be mentioned that the registration of undersampled volumes is a non-

trivial problem, due, among other technical issues, to the artifact level connected to the undersampling. However, with the introduction of sparse reconstruction techniques, which exploit correlations between images in the series to reduce the number of k-space points required to reconstruct each individual image (21,22), the image quality of such subsets may potentially be enhanced, so that image registration and corrected reconstruction may no longer be needed.

Recently, a novel image reconstruction framework, called eXtra-Dimensional Golden-angle RAdial Sparse Parallel (XD-GRASP) MRI, was proposed, which combines the acceleration capabilities of reduced k-space sampling and sparse reconstruction with the self-navigation properties of a hybrid radial and Cartesian (stack-of-stars) sampling scheme to reconstruct additional motion dimensions for dynamic liver imaging and cine cardiac imaging (23). Three-dimensional whole-heart coronary MRA is a static acquisition, rather than dynamic, but it can be an ideal extension for XD-GRASP, since the data acquired during free-breathing can be sorted and binned into multiple respiratory phases. This generates a fourth dimension, which represents the respiratory motion. As in the original XD-GRASP implementation, the new respiratory dimension can be regarded as an additional temporal correlation that can be exploited using a sparsity-based approach to reconstruct a 4D dataset (3D + respiratory dimension). Nevertheless, to extend this approach and achieve the whole-heart coverage and high isotropic spatial resolution needed for free-breathing coronary imaging, a 3D golden angle radial sampling scheme, which has recently been proposed (24), was utilized. This sampling scheme not only enables the flexible a posteriori combination of k-space segments needed for the respiratory binning, but also provides additional incoherence when compared to the original XD-GRASP implementation.

We therefore hypothesize that such sparse reconstruction algorithms can be exploited to reconstruct respiratory motion-resolved 3D images of the heart without the need for breath-holding, navigators, self-navigated respiratory correction, or complex 3D motion correction.

METHODS

A general schematic representation of the acquisition and reconstruction pipeline is displayed in Figure 1. Details about each step of the pipeline are provided in the sections below.

Data Acquisition

Written informed consent was obtained from all participants for this institutional review board–approved study. Volunteer and patient data acquisitions were performed using a prototype segmented 3D radial trajectory (24). Such a trajectory is subjected to a golden angle rotation about the z-axis at each heartbeat, such that each acquired segment is intrinsically positioned within the largest k-space void left by the prior segments. Additionally, a readout with consistent superior-inferior (SI) orientation at the beginning of each segment can be used for either respiratory self-navigation (10) or respiratory data binning (25). Because of the unique golden angle rotational arrangement of the readouts, it is possible to retrospectively sort (bin) all segments according to the respiratory phases (motion states) at which they were acquired. This results in distinct pseudo-uniform 3D k-space coverage for each respiratory bin.

Free-breathing whole-heart coronary MRA was performed in 11 healthy adult volunteers (9 male, mean age: 29 ± 4 years, range: 26–34 years) and, as a first proof of principle, in 4 patients (3 male, mean age: 64 ± 7 , range 54–72 years, sinus rhythm range 55–92 BPM) with established coronary artery disease (CAD). The acquisition was performed using ECG-triggering on a 1.5T clinical MRI scanner (MAGNETOM Aera, Siemens Healthcare GmbH, Erlangen, Germany) with a total of 30 receiver coil elements. For the volunteer group, the acquisition window (~ 80 – 100 ms / ~ 25 – 32 k-space lines per cardiac cycle) was placed in mid-diastole and adapted to the individual subject's heart rate using visual inspection of a 4-chamber cine dataset at high temporal resolution, while the scan was performed during approximately 400 heartbeats. For the patient group, the acquisition window was adapted to a shorter cardiac

rest phases ($\sim 40\text{-}60\text{ms}$ / 12-20 k-space lines per cardiac cycle), which was compensated for by an increased number of heartbeats (~ 600). The protocol parameters of the 3D radial, non-slice-selective, T_2 -prepared (TE T_2 -prep= 40ms), fat-saturated, bSSFP imaging sequence included: TR/TE 3.1/1.56ms, FOV (220mm)³, matrix 192³, voxel size (1.15mm)³, RF excitation angle 90°, and receiver bandwidth 898Hz/Pixel. The total amount of k-space lines acquired in each case was approximately 12000, for a total acquisition time of 7.0 ± 1.3 minutes.

Respiratory Motion Extraction

A recently described technique (25) that exploits signal amplitude variations from the center of k-space (KCA) (26) was adopted to extract respiratory-induced motion from all SI-oriented readouts. Since such variations have different contributions in each detector coil, the respiratory motion detection procedure (Figure 2) was repeated for all coil elements individually. Subsequently, independent component analysis (ICA) (27) was performed on the KCA signals from all coils to extract independent signal components. The signal component with maximum amplitude, within the bandwidth of the expected respiratory frequency (28), was used for respiratory binning.

Data Sorting

Figure 3a illustrates the data sorting procedure prior to XD-GRASP reconstruction. The whole-heart coronary MRA data, acquired using the 3D radial trajectory, were sub-divided into n sub-sampled 3D k-space datasets that originate from n different respiratory states. The number of k-space lines grouped in each individual state was the same. Due to the golden angle acquisition scheme, nearly uniform coverage of k-space was ensured for each bin and distinct sampling patterns among those bins are automatically obtained so that temporal incoherence and sparsity can be exploited in the iterative reconstruction. For the current study, $n = 4$ and 6 respiratory phases were used for data binning (Figure 3b&c). While a 6-phase subdivision of the breathing pattern leads to narrower and more sparsely populated bins (12,13), a 4-phase subdivision leads to wider bins that are more densely populated.

Both “4-phase XD-GRASP” and “6-phase XD-GRASP” reconstructions were performed, in order to investigate the effects of bin width on image quality.

According to prior experience (23), the regularization parameters of the XD-GRASP reconstruction were empirically optimized for 4- and 6-phase XD-GRASP on two representative training datasets by two coronary MRA experts (D.P. and M.S. with 7 and 20 years of experience in coronary MRA, respectively) blinded to the reconstruction parameters. Specifically, a range of values (from 0.005 to 0.1) of the regularization parameter were tested and visually compared. The values that generated the best image quality and coronary delineation were selected separately for the 4- and the 6-phase XD-GRASP reconstructions.

As the binning process is driven by the amount of data contained in each bin, the bin widths are not constant. As a consequence, the amount of motion included in each bin is also variable within the same subject. The relative amount of motion included in each bin or respiratory phase for the two binning approaches (4- and 6-phase) was measured as the percentage width of each bin relative to the entire respiratory excursion of a subject and these bin widths (expressed in %) were then averaged across all subjects. All values were reported as mean $\pm$ one standard deviation.

Image Reconstruction

XD-GRASP reconstruction was performed on all binned coronary datasets by solving the following optimization problem that enforces joint multicoil sparsity on the extra-dimensional dataset using a sparsifying transform along the new respiratory dimension:

$$d = \arg \min_d \|F \cdot C \cdot d - m\|_2^2 + \lambda \|S \cdot d\|_1 \quad [1]$$

Here, F is the non-uniform fast Fourier transform (NUFFT) operator defined for the 3D golden angle radial sampling pattern, and C represents the multiple-element coil sensitivity maps with dimensionality of x-y-z-coil, where x, y and z represent the three spatial dimensions. d is the respiratory motion-resolved image-series with dimensions x-y-z-t, and m represents the corresponding multicoil radial k-space data, sorted according to the respiratory state with dimension x-y-z-t-coil. The sparsifying transform S is

the first-order difference between respiratory states and the minimization of its l_1 -norm is commonly known as total variation (TV) minimization. This approach is well suited for applications where the image or volume is piecewise constant and it has performed well when compared to other, recently proposed sparsifying transforms (29). λ is the regularization parameter that weighs the contribution of the joint multicoil sparse regularization with respect to data consistency. Image reconstruction was implemented as described in (23) and the most end-expiratory volume was chosen for image analysis.

For comparison, each coronary dataset was also reconstructed using 1D respiratory self-navigation as described in (14). For respiratory self-navigation, respiratory motion was extracted by cross correlating the automatically segmented blood pool on the 1D FFT of an end-expiratory reference SI readout (reference SI projection) (15) to all other SI projections. The resulting 1D SI displacement was then used for correcting each data segment before the gridding operation, by directly applying a phase shift to all k-space readouts, and adapted for the polar orientation of each signal-readout. Image reconstruction was performed using a 3D regridding algorithm that makes use of a uniform density compensation function and a Kaiser-Bessel window. The multicoil 3D images were then combined using coil sensitivity maps estimated using the adaptive combination approach described in (30). A detailed description of the segmentation and cross-correlation algorithms can be found in (14).

All reconstructions were performed using a server equipped with two 16-core Opteron CPUs, 256Gb RAM, and two 6Gb NVIDIA graphics processing unit (GPU) cards. The NUFFT operation was implemented using parallel computing on GPUs (31), while the main reconstruction program was implemented in MATLAB 2012b (Mathworks, Natick, MA, USA).

Volunteer Study

All 1D respiratory self-navigated and end-expiratory phases of XD-GRASP reconstructed volunteer datasets were pooled, anonymized and randomized prior to image analysis.

Quantitative Assessment

To objectively determine the quality of vessel depiction, the proximal- and mid- segments of both the right coronary artery (RCA) and of the left anterior descending coronary artery (LAD) as well as the left main stem (LM) and the proximal left circumflex coronary artery (LCX) were identified on all datasets, as described in (32). The percentage vessel sharpness was computed for each of these segments as described in (33). The total visible vessel lengths were also measured for both the left coronary system (sum of LM and LAD) and the RCA.

Image Quality Assessment

On all datasets, the image quality of the entire LM, the proximal-, mid- and distal- segments of the LAD and of the RCA, and the proximal-LCX were graded on a 5-point scale similar to that described by Mc Connell et al (34). The two above-described experts performed this grading (image quality grading) using consensus reading (3). The scale classifies the definition of the vessel borders as follows: 0= not visible, 1=markedly blurred, 2=moderately blurred, 3=mildly blurred and 4=sharply defined. The average values of the quality grading, as well as the number of equal or higher scores in either of the two techniques were recorded.

Diagnostic Quality Assessment

Additionally, the diagnostic quality and visibility of each segment of LM, LAD, RCA, and proximal-LCX were graded for all coronary datasets on a 3-point scale (diagnostic quality grading) by an experienced cardiovascular MR radiologist (R.P.L. with 10 years of experience), blinded to the type of reconstruction. The scale used was: 0=non-visible, 1=visible, but non-diagnostic and 2=diagnostic.

Statistical Analysis

Statistical comparisons for the vessel sharpness and length were performed with a paired two-tailed Student's t-test in Excel (Microsoft, WA) and $p < 0.05$ was considered statistically significant. As for the quality grading and for the diagnostic grading, a nonparametric paired two-tailed Wilcoxon signed-rank test was used to compare the scores on a per vessel segment basis, as well as all scores for all segments of all patients considered together. Finally a McNemar's statistical test was used to assess statistical significance for the number of coronary segments that were graded as diagnostic with the three reconstructions. Bonferroni correction was applied where needed to correct for the multiple comparisons.

Initial Data Collection in Patients

Patient data were reconstructed using the 4-phase XD-GRASP reconstruction, and, because of the small sample size, the results were only visually compared to 1D respiratory self-navigation. Identification of the location of coronary stenoses on MRI was also visually compared to the findings from the gold-standard X-ray coronary angiography. These analyses were performed by D.P. and M.S.

RESULTS

Data Sorting

A 4-phase XD-GRASP reconstruction was found to be sufficient for resolving respiratory motion, and a regularization parameter of $\lambda = 0.02$ led to an optimal balance between removal of undersampling artifacts and reconstructed image quality. A 6-phase XD-GRASP reconstruction achieved similar performance with a higher regularization parameter ($\lambda = 0.05$) to account for the higher degree of undersampling. The relative amount of respiratory displacement for each of the bins was the smallest for the end-expiratory phase with $14.6 \pm 4.8\%$ and $8.2 \pm 2.8\%$ of the total motion for the 4-phase and 6-phase reconstruction, respectively. The phases with largest respiratory displacement were measured around end-inspiration at $35.3 \pm 8.0\%$ for the 4-phase XD-GRASP and $27.1 \pm 7.4\%$ for the 6-phase counterpart. Figure 4 shows images from one representative volunteer, where

conventional gridding reconstructions with sensitivity weighted multicoil combination for each respiratory phase, after binning, are visually compared with those obtained from 4-phase XD-GRASP. As evidenced by a gradual shift of both the heart and the liver in these images, respiratory motion can be resolved and accounted for by sorting the data into different motion states, while undersampling artifacts are efficiently removed with XD-GRASP reconstruction. Image quality of the motion states improves considerably using XD-GRASP, while the image registration step is no longer needed.

Image Reconstruction

The whole-heart coronary MRA acquisitions and reconstructions were successful for all volunteer and patient scans. The average reconstruction time for XD-GRASP was 35.1 ± 4.5 min (4-phase) and 58.2 ± 5.6 min (6-phase). By comparison, the 1D respiratory self-navigation inline reconstruction on the scanner lasted < 2 min.

Volunteer Study

An overview of the numerical results of image quality grading, vessel sharpness and length measurements is reported in Table 1.

Quantitative Assessment

Greater or equal vessel sharpness with respect to 1D respiratory self-navigation was obtained in 56/66 and 49/66 coronary segments and the total visible vessel length was superior or equal in 17/22 and 15/22 evaluated coronary arteries for the 4- and the 6-phase XD-GRASP reconstructions, respectively. The average vessel sharpness and length were superior for both XD-GRASP reconstructions with respect to 1D respiratory self-navigation. 4-phase XD-GRASP vessel sharpness was significantly superior to 1D respiratory self-navigation for the LM ($p < 0.003$), proximal- and mid-LAD ($p < 0.04$ and $p < 0.007$), and mid-RCA ($p < 0.008$). Visualized length of LM+LAD ($p < 0.05$) was also improved. Statistically significantly superior results for the 6-phase XD-GRASP reconstruction were achieved for the sharpness values of the mid-RCA ($p < 0.005$), when compared to 1D respiratory self-navigation. Figure 5 shows multiplanar reformats of the coronary arteries from one

representative volunteer: although 1D respiratory self-navigation already led to adequate image quality (Figure 5a), a clear improvement in sharpness and visible vessel length (white arrows) can be appreciated in both the 4-phase and 6-phase XD-GRASP reconstructions.

Image Quality Assessment

In the vast majority of cases, the respiratory-resolved XD-GRASP reconstruction achieved equal or improved image quality grades relative to 1D respiratory self-navigation. In particular, the quality grade was greater or equal in 76/88 and in 80/88 coronary segments for the 4- and 6-phase XD-GRASP reconstructions, respectively. The average grade of the qualitative assessment was superior for both XD-GRASP reconstructions, except for the quality grade of the proximal-LCX, which was very similar to that of 1D respiratory self-navigation. The paired two-tailed Wilcoxon signed-rank test showed statistical significance for the improvements in the image quality grades of all coronary segments considered together for both 4-phase XD-GRASP reconstruction ($p < 0.0001$) and 6-phase XD-GRASP reconstruction ($p < 0.0001$), when compared with 1D respiratory self-navigation. There was no statistically significant difference ($p = 0.06$) between the two XD-GRASP reconstructions. When looking at the per segment analysis, statistical significance was reached for the mid-LAD for the 4-phase XD-GRASP and for the mid-LAD, mid- and distal-RCA for the 6-phase XD-GRASP (Table 1).

Diagnostic Quality Assessment

The results related to the diagnostic grading are reported in Table 2. Overall, the ratio of coronary segments labeled as diagnostic increased from 41/88 for 1D respiratory self-navigation to 61/88 and 56/88 for the 4- and 6-phase XD-GRASP reconstructions, respectively. Conversely, the total ratio of non-visible segments decreased from 5/88, with 1D respiratory-self navigation, to 1/88 with both 4- and 6-phase XD-GRASP reconstructions. The diagnostic grades obtained for the 4-phase XD-GRASP reconstructions were higher or equal to those of 1D respiratory self-navigation in 87/88 coronary segments, while this ratio was 85/88 for 6-phase XD-GRASP. On average, the diagnostic grades for the XD-GRASP reconstructions were

always higher than those obtained with 1D respiratory self-navigation, with the only exception being the proximal-LCX. The 4-phase XD-GRASP reconstruction reached 100% diagnostic quality for LM, proximal-LAD, and proximal-RCA. Full diagnostic quality was also reached with the 6-phase reconstruction for LM and proximal-RCA.

The paired two-tailed Wilcoxon signed-rank test showed statistical significance for the improvements in the diagnostic quality grades of all coronary segments considered together for both 4-phase XD-GRASP reconstruction ($p < 0.0001$) and 6-phase XD-GRASP reconstruction ($p < 0.0005$) when compared to 1D respiratory self-navigation. The McNemar's statistical test showed that the increase in the number of diagnostic coronary segments was significant for both 4-phase ($p < 0.0001$) and 6-phase ($p < 0.003$) reconstructions, with respect to 1D respiratory self-navigation. Also in this case, a comparison between the 4-phase and 6-phase approach did not lead to statistically significant results.

A volunteer dataset where 1D respiratory self-navigation did not achieve diagnostic quality is shown in Figure 6. Although there is a visual improvement with respect to the uncorrected reconstruction (where gridding of all k-space lines was performed without any respiratory motion correction), the coronal view shows substantial residual blurring and only the proximal segments of LAD and LCX are visible. Even though a long contiguous segment of the RCA is displayed, diagnostic quality was not reached for the more distal segments. By contrast, using XD-GRASP reconstruction, sharp and well defined borders of coronary, myocardial and hepatic structures can be appreciated (arrowheads). Coronary segments that were graded as “visible, but non-diagnostic” on the 1D respiratory self-navigation were considered “diagnostic” after XD-GRASP reconstruction (arrows).

Initial Findings in Patients

All datasets were successfully reconstructed in this initial and small patient cohort. All patients had at least two-vessel coronary artery disease in the proximal or mid-segments as diagnosed by x-ray coronary angiography. In three of the four patients, one or more coronary stenoses were successfully visualized by MR. The image quality of the fourth patient was not sufficient to

confirm stenoses in the mid- and distal coronary segments. Importantly, the regularization term of the 4-phase XD-GRASP reconstruction did not affect the depiction of stenosis and the vessels appeared sharper than in the reformats from 1D respiratory self-navigation. Example reformats from one CAD patient are displayed in Figure 7. Both 1D respiratory self-navigation and 4-phase XD-GRASP reconstruction are shown in comparison to the gold standard x-ray coronary angiogram. A significant stenosis of the proximal LAD is well visualized in both the self-navigated and the XD-GRASP reconstruction (arrows).

DISCUSSION

XD-GRASP has previously been introduced as a sparse iterative reconstruction technique that can be exploited for motion suppression in dynamic MRI using a stack-of-stars sampling scheme (23). In the present study, the XD-GRASP framework was extended for free-breathing 3D whole-heart, coronary MRA. For this purpose, it was combined with a 3D golden-angle radial trajectory that does not only enable whole-heart coverage at high isotropic spatial resolution, but also a flexible a posteriori combination of k-space segments that are re-grouped into pseudo-uniform phases of bins.

Specifically, we tested the hypothesis that this approach can be leveraged to reconstruct respiratory motion-resolved 3D images of the heart without the need for navigators, self-navigated respiratory correction, or tailored models for 3D motion correction. A respiratory signal is extracted directly from the imaging data and used only for sorting the acquired data into multiple respiratory states. Although conventional gridding reconstruction of the individual bins may provide motion-resolved images, the considerable degree of undersampling would inevitably lead to noise and streaking artifacts. However, the correlation along the new respiratory dimension is well suited for reconstruction using the XD-GRASP framework. With this approach, image registration of low quality sub-images can be avoided, as the respiratory dimension is used to create a sparse time domain that can be exploited to enhance the image quality of each individual respiratory bin. Although the end-expiratory 3D volume of the XD-GRASP reconstruction was selected for

coronary artery visualization in our study, it should be noted that the reconstructed motion-resolved datasets contain abundant anatomic information across the whole respiratory cycle, which may be further exploited (Supplemental Material).

This approach was tested in a group of healthy adult volunteers and preliminarily in a small number of CAD patients, and was compared to 1D respiratory self-navigation. In this context, it is important to emphasize that the exact same acquired data were used, yet the reconstruction pathway was different. The results show that vessel conspicuity and vessel length were superior with the proposed methodology. While the image quality assessment was used to identify overall improvements in image quality, the diagnostic quality assessment answered to the question whether diagnostic quality of a vessel segment was obtained. Furthermore, initial patient data also demonstrated considerable promise for improved delineation of proximal coronary segments.

As conventional whole-heart coronary MRA is commonly performed with end-expiratory navigator-gating that suffers from variable scan efficiency and unpredictable scanning times, several groups have proposed the acquisition of data during the entire respiratory cycle, together with aggressive motion correction to obtain reduced and predictable scan times (9-11). In most cases, respiratory motion is retrospectively corrected using registration algorithms (12,13,18,35). However, the motion correction performed using specific motion models (11,13,36,37) remains an approximation of the real respiratory-induced motion of the heart. Hypothetically, this limitation promises to be intrinsically addressed using the XD-GRASP methodology, since neither motion models nor registration algorithms are required. Nevertheless, a direct comparison between the proposed motion-resolved reconstruction approach and established techniques based on navigator gating will be required to test this hypothesis. However, the 1D self-navigation technique has already been compared to the standard navigator-gated technique in volunteers (10) and similar image quality was obtained. For this reason, and because of scan time constraints, a direct comparison between the XD-GRASP technique and a standard navigator-gated technique was not added to the present study.

An important aspect also relates to the tradeoff between the number of reconstructed respiratory phases and the residual, intra-bin, sparsity artifacts. Here, XD-GRASP reconstruction was performed with both 4 and 6 respiratory phases. Although the use of a larger number of respiratory phases might be expected to better resolve respiratory motion and reduce blurring, a higher number of phases is also associated with increased degrees of undersampling in each of them. The results suggest that, for our healthy volunteer cohort, both 4-phase and 6-phase XD-GRASP reconstructions are very similar in performance. Ideally, the number of reconstructed respiratory phases could be tailored to the specific breathing pattern of each subject, choosing, for example, less phases for more regular breathers, where the overall respiratory displacement is relatively small, and more phases for irregular breathers, where the total respiratory amplitude may be larger (38). Although the results obtained in the initial patient cohort seem to confirm that a 4-phase reconstruction might be sufficient also for this population, the number of subjects is too small and the link between respiratory drift or irregular breathing and an optimal reconstruction yet remains to be ascertained. Further analyses on a larger patient population would be useful to investigate the relationship between the different breathing patterns and the optimal number of reconstructed phases.

Although sparse reconstruction techniques have previously been applied for whole-heart coronary MRA (20,39-43), most of the implementations aim at reducing the acquisition time by exploiting spatial correlations. XD-GRASP, on the other hand, sorts the acquired data into an additional respiratory dimension and exploits sparsity in this new dynamic dimension. The high correlation in this respiratory dimension enables improved performance in XD-GRASP reconstruction when compared to conventional sparse reconstructions exploiting spatial correlation only.

The golden-angle arrangement of the 3D radial phyllotaxis trajectory intrinsically facilitates the extraction of the respiratory motion signal directly from the image data (since all readouts cross the k-space center) and provides flexibility in data sorting (since quasi-uniform spatial sampling over time – and therefore in all respiratory bins – is facilitated). Simultaneously, the golden angle rotation ensures a certain level of incoherence along the new

respiratory dimension, which is required for XD-GRASP reconstruction (i.e., the data are sufficiently distinct in different motion states, since the same k-space profile is never acquired twice).

In ECG-triggered whole-heart coronary MRA, data acquisition is typically performed during a short acquisition window in diastole. However, 4D cardiac and respiratory motion-resolved whole-heart coronary MRA approaches have recently been proposed (44,45), which advocate continuous data acquisition through the entire cardiac cycle. Coronary artery images can be reconstructed at different cardiac phases and additional information on 3D cardiac function can be extracted. The extension of these 4D approaches with XD-GRASP seems straightforward, and it would enable simultaneous exploitation of correlations in both cardiac and respiratory dimensions, thus leading to 5D cardiac MRI.

Two limitations of our initial proof-of-concept implementation include: 1) lengthy reconstruction times due to the iterative reconstruction process, which requires the computation of one forward and one inverse 3D non-uniform fast Fourier transform (NUFFT) for each respiratory phase and coil per iteration, and 2) substantial memory requirements to respond to the computational needs associated with large, high-resolution 3D datasets. However, with continued progress in computer hardware and software, this is not likely to be a future roadblock. While this study had a strong focus on coronary MRA with most stringent boundary conditions because of the small and tortuous nature of the vessels, the XD-GRASP approach will likely benefit other 3D cardiac imaging techniques such as delayed hyperenhancement studies as well as T1- and T2 mapping. Finally, XD-GRASP may potentially be combined with methods that simultaneously exploit the spatial sparsity of the images. Based on earlier numerical simulations (29), only a moderate improvement in image quality is expected and an increasing degree of freedom for optimization of the regularization weights will have to be considered.

CONCLUSIONS

A powerful alternative to navigators or self-navigation for handling respiratory motion in 3D whole-heart coronary MRA has been proposed. The

XD-GRASP framework can be exploited to reconstruct respiratory motion-resolved 3D images of the heart without the need for breath-holding, navigators, self-navigated respiratory motion correction, or complex 3D correction schemes.

Instead of discarding data segments from inconsistent respiratory phases or enforcing motion models for motion correction that are inevitably imperfect, XD-GRASP makes constructive use of all respiratory phases to improve image quality, and achieves superior image quality compared to 1D respiratory self-navigation. A 3D radial phyllotaxis trajectory and XD-GRASP reconstruction provide a synergistic combination that ultimately may lead coronary MRA closer to clinical practice.

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Table 1 – Quality grading and quantitative assessment: Average values of the image quality grades, vessel sharpness and length for the 11 volunteers and using 1D respiratory self-navigation as compared with the proposed respiratory-resolved XD-GRASP reconstruction (LM = left main stem, LAD = left anterior descending artery, LCX = left circumflex artery, and RCA = right coronary artery).

Coronary Segment	Measured Parameter	1D Self-Navigation	4-Phase XD-GRASP	6-Phase XD-GRASP
LM:	Image Quality Grading	1.8±0.8	2.0±0.5	2.1±0.5
	Sharpness [%]	48.4±7.7	55.1±7.7*	49.1±8.5
LAD (Prox):	Image Quality Grading	1.5±0.8	1.9±0.5	2.0±0.6
	Sharpness [%]	37.3±8.6	41.9±8.1*	40.2±7.7
LAD (Mid):	Image Quality Grading	1.0±0.8	1.5±0.4*	1.5±0.6*
	Sharpness [%]	34.9±10.2	40.8±9.1*	38.7±8.7
LAD (Dist):	Image Quality Grading	0.8±0.6	1.1±0.6	1.2±0.8
LM+LAD	Length [cm]	11.7±3.2	13.2±3.1*	12.8±3.1*
LCX (Prox):	Image Quality Grading	1.1±0.7	1.0±0.5	1.0±0.5
	Sharpness [%]	43.2±9.3	46.3±12.9	48.7±7.9
RCA (Prox):	Image Quality Grading	1.9±0.7	2.2±0.4	2.3±0.5
	Sharpness [%]	46.9±11.0	53.2±5.3	52.5±5.6
RCA (Mid):	Image Quality Grading	1.7±0.6	2.0±0.4	2.2±0.7*
	Sharpness [%]	42.9±10.4	49.8±6.2*	49.9±7.5*
RCA (Dist):	Image Quality Grading	1.2±0.8	1.5±0.4	1.7±0.7*
RCA	Length [cm]	11.2±2.5	12.1±1.6	11.7±3.1
All values are expressed as mean ± one standard deviation * Indicates statistical significance compared to 1D Respiratory Self-Navigation. Image Quality Grading: 0 = not visible, 1 = markedly blurred, 2 = moderately blurred, 3 = mildly blurred and 4 = sharply defined. LM = Left Main Artery, LAD = Left Anterior Descending Artery, LCX = Left Circumflex Coronary Artery, RCA: Right Coronary Artery				

Table 2 – Diagnostic quality grading: Average values of the diagnostic quality grades for the 11 volunteers, using 1D respiratory self-navigation as compared with the proposed XD-GRASP reconstruction. A clear improvement can be seen in the datasets where respiratory-resolved XD-GRASP reconstruction was applied (LM = left main stem, LAD = left anterior descending artery, LCX = left circumflex artery, and RCA = right coronary artery).

Coronary	Segment	1D Respiratory Self-Navigation	4-Phase XD-GRASP	6-Phase XD-GRASP
LM:	-----	1.8±0.4	2.0±0.0	2.0±0.0
LAD:	Prox.	1.6±0.5	2.0±0.0	1.7±0.5
	Mid	1.3±0.6	1.4±0.5	1.5±0.5
	Dist.	0.9±0.5	1.3±0.5	1.3±0.5
LCX:	Prox.	1.4±0.7	1.4±0.7	1.4±0.7
RCA:	Prox.	1.8±0.4	2.0±0.0	2.0±0.0
	Mid	1.3±0.5	1.7±0.5	1.5±0.5
	Dist.	1.4±0.7	1.7±0.5	1.6±0.5
Total Diagnostic Segments		41/88 (47%)	61/88 (70%)*	56/88 (63%)*
All values are expressed as mean ± one standard deviation * Indicates statistical significance compared to 1D Respiratory Self-Navigation. Diagnostic Quality Grading: 0 = non-visible, 1 = visible but non diagnostic and 2 = visible and diagnostic LM = Left Main Artery, LAD = Left Anterior Descending Artery, LCX = Left Circumflex Coronary Artery, RCA: Right Coronary Artery				

FIGURE CAPTIONS

Figure 1: Schematic representation of the acquisition / reconstruction pipeline proposed in this work. The flow chart shows how the radial k-space lines of the whole heart coronary MRA datasets are acquired with a 3D radial acquisition scheme, as opposed to the 2D radial stack of stars scheme proposed in the original publication. The acquired static data are first used for respiratory motion extraction and then consequently binned into distinct respiratory phases via the data sorting procedure. The sorted data are then fed into the XD-GRASP sparse iterative reconstruction algorithm to generate the final respiratory motion resolved dataset. Coil sensitivity maps are also directly extracted from the radial acquisition and subsequently used in the iterative reconstruction.

Figure 2: Procedure for respiratory motion detection. First, separate components of the k-space center amplitude (KCA) signal are extracted from the SI readouts for each receive coil element (a). Subsequently, Independent Component Analysis (ICA) is performed on all KCA signals to identify different independent components. The component with highest amplitude in the frequency range of respiration (b: black line) is then selected and used as the respiratory motion signal for data sorting into respiratory bins.

Figure 3: Data sorting procedure for XD-GRASP reconstruction. The whole-heart coronary MRA dataset acquired using the phyllotaxis 3D radial trajectory can be binned into any number n of respiratory phases, spanning from end-expiration (top) to end-inspiration (bottom), using the motion signal detected as illustrated in (a). Each dot represents the origin – on the top half of k-space – of a linear readout going through the center of k-space. The binning procedure is then performed so that the number of spokes grouped in each respiratory phase is equal, therefore leading to different bin widths. Due to the golden angle acquisition scheme, approximately uniform coverage of k-space with distinct sampling patterns in each phase is always achieved (b,c). Two examples of data binning with four (b) and six (c) separate phases are shown.

Figure 4: Example from one representative healthy adult volunteer comparing conventional sensitivity weighted multicoil gridding reconstruction with the 4-phase XD-GRASP reconstruction. All reconstructed phases are shown in an axial plane (top) and a coronal plane (bottom). Respiratory motion is resolved by sorting the data into different motion states, while the streaking artifacts due to undersampling are effectively removed in the XD-GRASP reconstruction.

Figure 5: Examples of multiplanar reformatted coronary arteries from one representative healthy adult volunteer. Although respiratory self-navigated reconstruction with 1D motion correction could achieve high image quality (a), a clear improvement in sharpness as well as visible vessel length (white arrows) can be noticed in both 4-phase (b) and 6-phase (c) XD-GRASP reconstructions.

Figure 6: Example of a selected healthy adult volunteer dataset in which 1D respiratory self-navigation did not lead to diagnostic image quality. Although a clear improvement can be noticed from the uncorrected reconstruction to 1D respiratory self-navigation, the coronal view still shows strong residual blurring after conventional respiratory motion correction. Only the proximal segments of LAD and LCX are visible, while the RCA, although visible, was not scored with full diagnostic quality in the mid and distal segments. By contrast, the dataset provided by the XD-GRASP reconstruction shows sharp and well defined margins of a papillary muscle in the left ventricle and of the liver on the coronal view (white arrow heads). All coronary arteries are better depicted and an increased vessel length can be visualized with the XD-GRASP reconstruction. Coronary segments graded as only “visible” in the 1D respiratory self-navigation are depicted with “diagnostic quality” with the proposed XD-GRASP methodology (white arrows).

Figure 7: Sample images from a selected patient dataset. Both 1D respiratory self-navigation and the 4-phase XD-GRASP reconstruction can be directly compared to the standard 2D X-ray angiogram. The X-ray angiogram shows a

significant stenosis of the proximal LAD, which is also well visualized in the corresponding self-navigated dataset (arrows). The 4-phase XD-GRASP reconstruction does not affect depiction of the stenosis (arrow), while the vessel itself appears to be even sharper. The signal void present on MR images distal to the stenosis is caused by the presence of a coronary stent in the proximal LCX.

Supporting Material: Example of a complete respiratory-resolved whole-heart dataset from one of the volunteers. The animation scrolls through all slices of the datasets in the three standard orientations: (a) transversal, (b) coronal, and (c) sagittal, while all respiratory motion states are displayed for each slice. Although only the most end-expiratory state was used for the qualitative and quantitative comparisons, the XD-GRASP reconstruction provides one volume with high and isotropic spatial resolution for each respiratory motion state.

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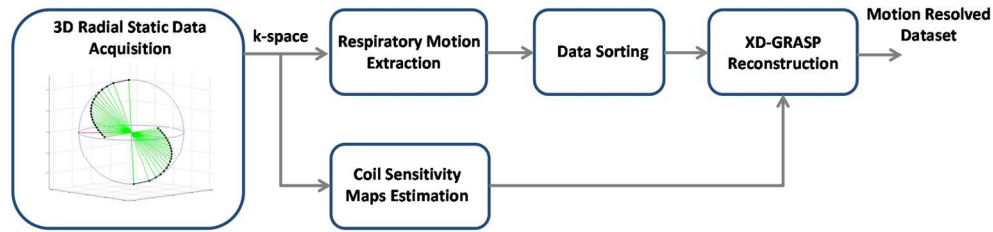


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174x40mm (300 x 300 DPI)

Accepted

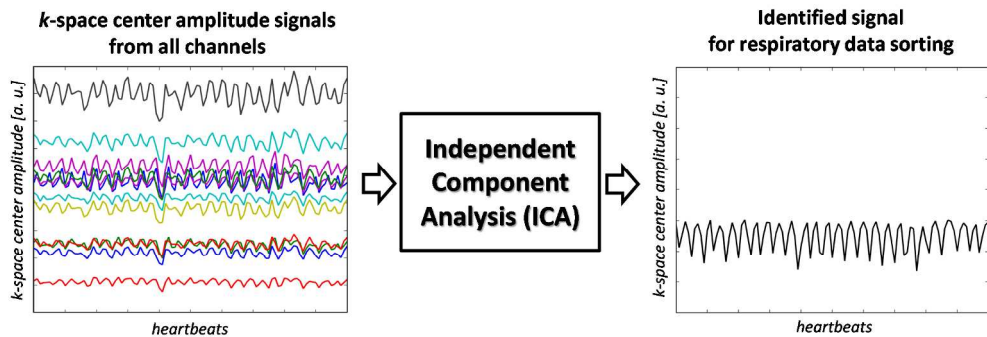


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844x288mm (600 x 600 DPI)

Accepted

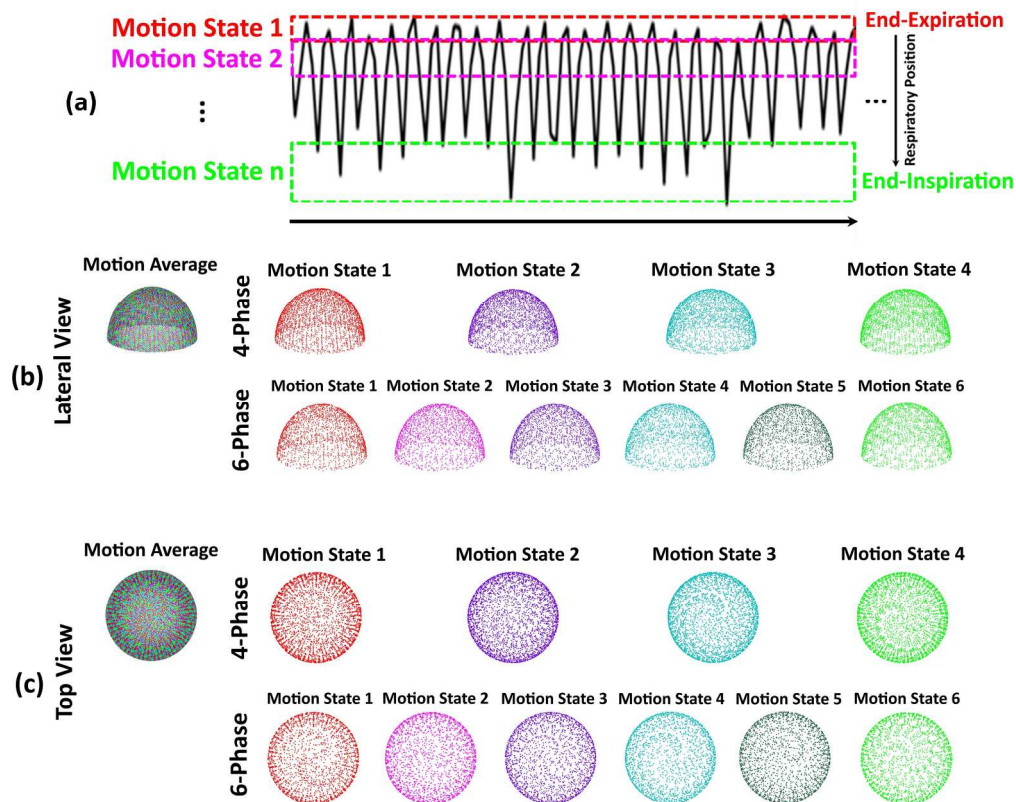


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AC

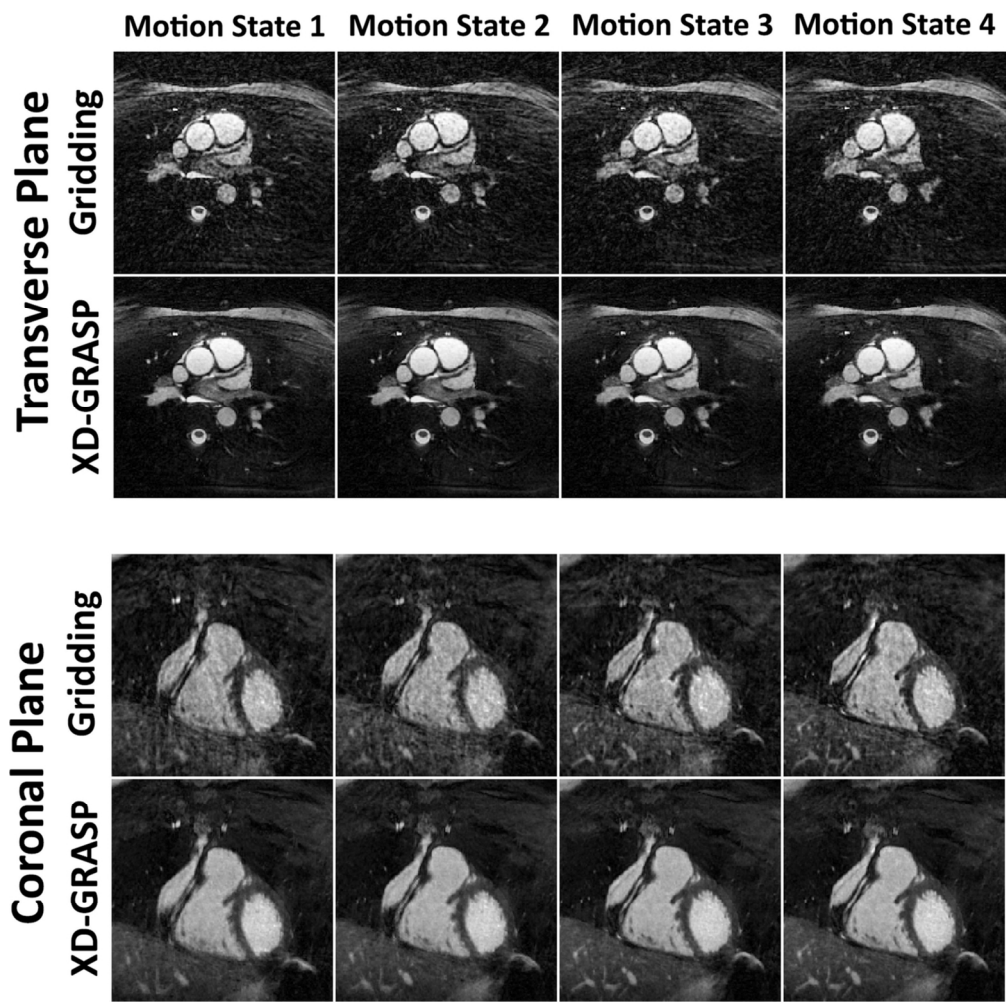


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A

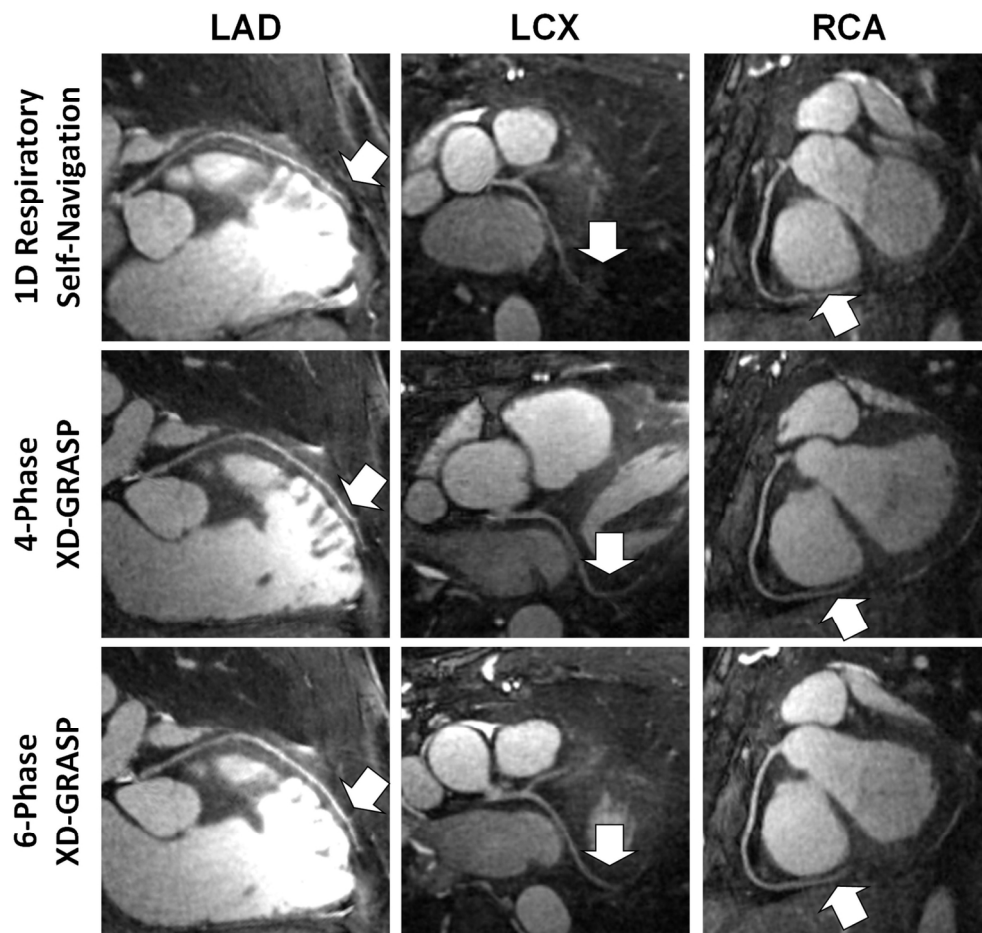


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AC

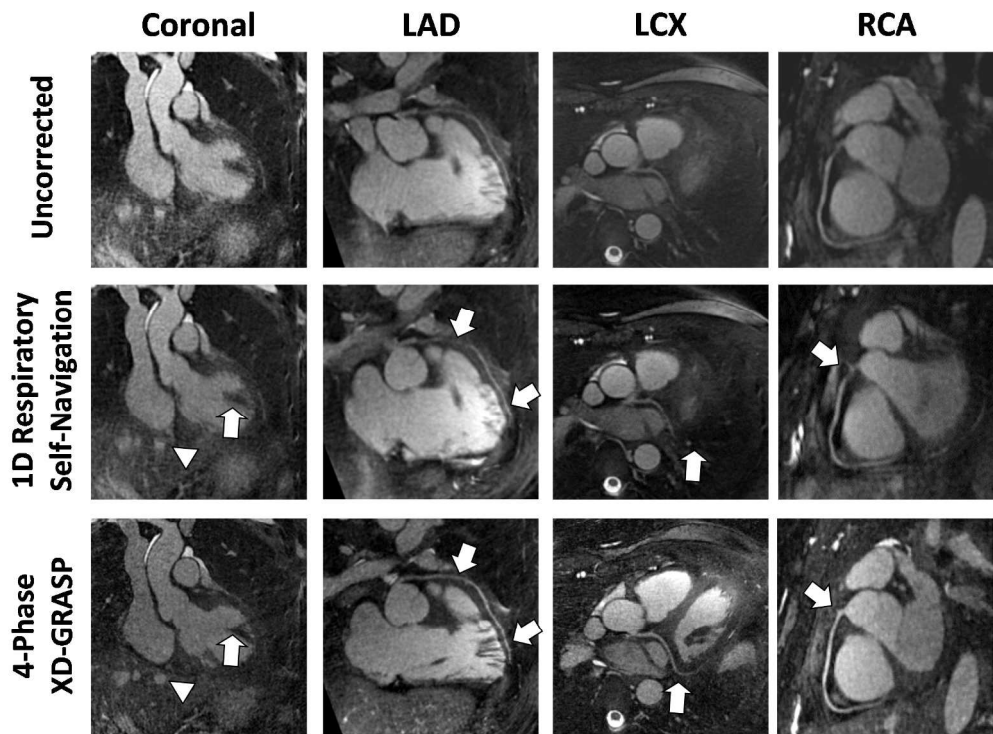


Figure 6: Example of a selected healthy adult volunteer dataset in which 1D respiratory self-navigation did not lead to diagnostic image quality. Although a clear improvement can be noticed from the uncorrected reconstruction to 1D respiratory self-navigation, the coronal view still shows strong residual blurring after conventional respiratory motion correction. Only the proximal segments of LAD and LCX are visible, while the RCA, although visible, was not scored with full diagnostic quality in the mid and distal segments. By contrast, the dataset provided by the XD-GRASP reconstruction shows sharp and well defined margins of a papillary muscle in the left ventricle and of the liver on the coronal view (white arrow heads). All coronary arteries are better depicted and an increased vessel length can be visualized with the XD-GRASP reconstruction. Coronary segments graded as only "visible" in the 1D respiratory self-navigation are depicted with "diagnostic quality" with the proposed XD-GRASP methodology (white arrows).

588x436mm (600 x 600 DPI)

ACC

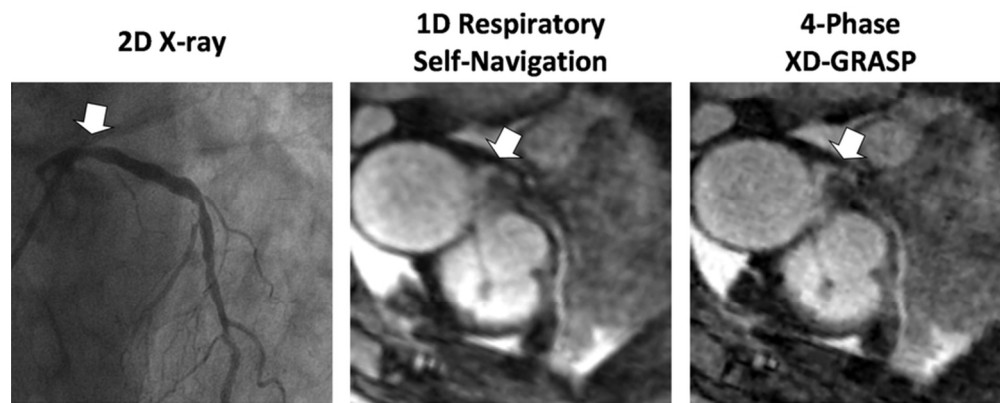


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Accepted