

Self-Navigated Tissue Phase Mapping Using a Golden-Angle Spiral Acquisition – Proof of Concept In Patients With Pulmonary Hypertension

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ABSTRACT

Purpose: To create a high temporal- and spatial-resolution retrospectively cardiac-gated, tissue phase mapping (TPM) sequence, using an image-based respiratory navigator calculated from the data itself.

Methods: The sequence was based on a golden-angle spiral acquisition. Reconstruction of real-time images allowed creation of an image-based navigator. The expiratory spiral interleaves were then retrospectively cardiac-gated using data binning. TPM data was acquired in 20 healthy volunteers and 10 patients with pulmonary hypertension. Longitudinal and radial myocardial velocities were calculated in the left ventricle (LV) and right ventricle (RV).

Results: The image-based navigator was shown to correlate well with simultaneously acquired airflow data in 10 volunteers ($r=0.93\pm 0.04$). The TPM navigated images had a significantly higher subjective image quality and edge sharpness ($P<0.0001$) than averaged spiral TPM. No significant differences in myocardial velocities were seen between conventional Cartesian TPM with navigator respiratory-gating and the proposed self-navigated TPM technique, in 10 volunteers. Significant differences in the velocities were seen between the volunteers and patients in the LV at systole and end diastole, and in the RV at end diastole.

Conclusion: We have demonstrated the feasibility of measuring myocardial motion using a golden-angle spiral TPM sequence, with an image-based respiratory navigator calculated from the TPM data itself.

Key words: Tissue Phase Mapping, Myocardial Motion, Golden-angle, Image-based Self-Navigation

INTRODUCTION

Magnetic resonance tissue phase mapping (TPM) allows assessment of the separate directional components of wall motion, as well as their regional distribution. However, the requirement for velocity encoding in all three directions results in long acquisition times. This is particularly true when imaging the thin walled right ventricle (RV), as higher spatial-resolution is also required. Thus, the majority of TPM implementations are acquired during free-breathing, with respiratory navigators used to reduce respiratory motion artifacts (1-3).

Conventional respiratory navigation can be carried out in multiple ways, including the use of a pencil beam excitation through the diaphragm or Prospective Acquisition Correction (PACE) (4). These techniques require a break in data acquisition and for this reason they are usually combined with prospective cardiac gating. Unfortunately, this acquisition schema leads to a loss of information in some parts of the cardiac cycle. A better approach might be self-gating, in which the respiratory signal is extracted from the TPM data itself. The benefits of self-gating are that there are no gaps in data acquisition and hence it lends itself to retrospective cardiac-gating.

One method of self-gating is to acquire data in such a way that real-time images can be reconstructed from the data itself and used to calculate an image-based navigator (5,6). However, efficient k-space filling or data undersampling is required to produce real-time images at sufficient temporal-resolution to capture respiratory motion. One possibility is to combine undersampled spiral trajectories with a Sensitivity Encoding (SENSE) reconstruction (7). However, to ensure that the final gated data is not as undersampled as the real-time images, the interleaves must be rotated with each real-time frame. In such a scheme, the uniformity of k-space filling in the cardiac-gated data will depend on the exact angle of rotation. For arbitrary temporal-resolutions, a golden-angle rotation strategy is the optimum method of guaranteeing uniform filling of k-space (8-10). Therefore, this strategy may also provide more uniform k-space filling of respiratory-navigated, retrospectively cardiac binned TPM data.

In this study, we implemented a golden-angle spiral TPM sequence, in which the data was first reconstructed as real-time images to produce an image-based navigator. The navigator was then used to select the spiral interleaves acquired in expiration, for final reconstruction of the retrospectively cardiac-gated data. The aims of this study were; i) To demonstrate that it is possible to derive an image-based navigator from the real-time data itself, which can be used to perform respiratory gating allowing an improvement in image quality; ii) To show that the golden-angle strategy resulted in more uniform filling of the respiratory-navigated, retrospectively cardiac-gated k-space; and iii) To demonstrate that it is feasible to measure clinical relevant myocardial velocities in the left ventricle (LV) and right ventricle (RV) of both normal controls and patients with pulmonary hypertension (PH).

METHODS

Study Population

The study population consisted of 20 healthy volunteers (14 male, 6 female: median age 35.1 ± 6.3 years, range: 24.2 to 47.0 years) and 10 patients with known pulmonary hypertension (3 male, 7 female: median age 51.3 ± 13.5 years, range: 31.3 to 74.0 years). Exclusion criteria were; i) Irregular heart rates i.e. multiple ectopic beats or atrial fibrillation; ii) Contraindications to MR such as MR-incompatible implants; or iii) Pregnancy. The local research ethics committee approved the study and written consent was obtained from all volunteers and patients.

All imaging was performed on a 1.5T MR scanner (Magnetom Avanto, Siemens Medical Solutions, Erlangen, Germany) using two rows of spine coil elements and two rows of body-matrix elements, giving a total of 12 coil elements. A vector electrocardiographic (ECG) system was used for cardiac-gating. In all subjects the proposed self-navigated TPM technique was performed in the short axis orientation at the mid-ventricular position, with all reconstructions performed in the Siemens reconstruction environment. The volunteer population was divided into two subgroups; in the first subgroup (N=10) respiratory airflow was measured during the proposed TPM acquisition using an MR compatible flow meter (Biopac MP Systems, California, USA) connected to an airtight mask; and in the second subgroup (N=10) an additional conventional Cartesian TPM acquisition was performed (in the same imaging plane as the proposed TPM acquisition, optimized to have a similar spatial and temporal resolution) with navigator respiratory gating (PACE, with an acceptance window of 4 mm). The first subgroup allowed us to assess the correlation of airflow with the image-based navigator. The second subgroup allowed us to compare velocities measured from the conventional Cartesian acquisition, the averaged spiral TPM data, and the self-navigated spiral TPM data.

Tissue Phase Mapping Acquisition

The proposed TPM acquisition was based on a uniform density spiral, three-directional phase-contrast sequence (see Figure 1). The spiral design was based on that described

by Hargreaves, et al. (11) with each interleave lasting 8.31 ms (consisting of 5935 samples with a dwell time of 1.4 μ s, with an oversampling factor of 2). A *two-sided* flow-encoding scheme was used (12) with positive and negative bipolar pulses applied for each velocity-encoding direction (a 'flow-encoding couplet'). Thus to measure flow in three directions, six flow-encoded readouts must be acquired. This is different from a conventional scheme in which four readouts are necessary. The benefit of this two-sided flow-encoded scheme is that the temporal-resolution is higher, as each flow-encoded couplet is independent. Each consecutive flow-encoding couplet was rotated by the golden-angle, as previously described (9). The velocity sensitivity was set to 30 cm/s to ensure no velocity aliasing occurred within the myocardium, to maintain a reasonable TE and to reduce background offsets caused by eddy currents.

Data was continuously acquired to allow the theoretical acquisition of a fully sampled k-space with 40 spiral interleaves, for each of the three flow-encoded directions, within all 40 cardiac phases, with a cardiac-gating oversampling factor of 20%, in addition to a respiratory navigation efficiency of 30% (see Table 1 for all imaging parameters). Theoretically, to acquire 40 spiral interleaves in all 40 frames, for the six flow-encoded readouts, with a TR of 13.6 ms, requires 130.56 s. Including the 20% oversampling and using a 30% respiratory navigator efficiency, the total scan time was therefore ~8.7 minutes.

Real-time Image Reconstruction

Real-time images were reconstructed from 10 consecutive flow-encoding couplets (resulting in a temporal-resolution of the real-time images of ~270 ms). As this resulted in an undersampled k-space (acceleration factor: ~4), an iterative non-Cartesian SENSE algorithm was used for image reconstruction (7). The stopping criterion for the algorithm was a residual of less than 10^{-3} , which resulted in ~12 iterations. The necessary coil sensitivity maps were acquired with the same imaging parameters as the tissue phase mapping sequence in a pre-scan, over ~11 seconds to ensure a high signal-to-noise ratio and acquisition of data during inspiration and expiration.

Calculation of the Respiratory Navigator

The image-based respiratory navigator was calculated by cross-correlating the real-time series with five real-time frames selected from end-expiration. The expiratory frames were identified by projecting the real-time series onto the x- and y-axes, and calculating the center-of-mass. The two center-of-mass signals were then tested for respiratory power in the frequency domain, with the highest being used for further analysis. The five most anterior or superior positions (depending on the axis) in the center-of-mass signal were considered to be coincident with end-expiration. Cross-correlation with these expiratory frames produced five separate navigator signals, which were then averaged and Fourier interpolated. We choose a ten-fold interpolation to ensure that each of the flow-encoding couplets was associated with an individual point in the navigator signal. Thirty percent of flow-encoding couplets associated with the highest correlation coefficients (i.e. the most expiratory positions) were then used in the final, cardiac-gated TPM image reconstruction (see *Figure 2*).

In the first volunteer subgroup (N=10), the navigator signal was correlated against simultaneously acquired airflow data. It was necessary to differentiate the navigator signal (13) in order to convert displacement to flow for comparison of the signals (MATLAB R2012a, The MathWorks Inc., Natick, MA).

Reconstruction of Gated TPM Data

The navigator-selected flow-encoding couplets in each velocity direction were binned into 40 phases depending on their linearly-normalized cardiac timestamp (14). As each k-space had a different number and distribution of interleaves, the resultant 120 k-spaces (40 phases, 3 velocity-encoding directions) were reconstructed using an iterative SENSE algorithm (with no density compensation for the non-uniform filling of the resultant k-spaces). The stopping criterion for the algorithm was a residual of less than 10^{-3} , which resulted in ~5 iterations for the final averaged TPM data and ~7 iterations for the final navigated TPM data.

In order to assess if the golden-angle strategy was an optimized method of filling k-space, it was necessary to simulate k-space filling using a more traditional rotation strategy. The simulated rotation strategy was similar to a previously described method used in real-time flow imaging (15). Briefly, each simulated real-time, k-space frame

contained 10 regularly spaced interleaves out of a possible 40 interleaves (acceleration factor: 4). In subsequent frames, all interleaves were rotated by 9° and therefore k-space was fully sampled every four frames. Using the linearly-normalized cardiac timestamps and calculated respiratory navigator from the volunteers, it was possible to simulate k-space filling if this conventional strategy was used. To assess the uniformity of k-space filling, it was necessary to produce a simple metric of the relative position of the spiral interleaves. One measure is the angle between adjacent interleaves, which should not vary when k-space is uniformly filled. Thus, the coefficient of variation (CoV) of these angles can be taken as a measure of non-uniformity of filling (where a lower CoV equates to more uniform filling). The mean CoV (across all frames and direction) for the golden-angle acquisition was compared to the CoV of simulated k-spaces to determine the most optimized method.

Image Quality Assessment

Image quality was assessed in the conventional Cartesian TPM data, as well as both the image-based, respiratory-navigated TPM data and a non-navigated, averaged reconstruction (signal average ~ 3).

Subjective image scoring was performed by two independent, experienced observers who were presented with the magnitude images in a blinded, randomized manner. The image quality was graded as; 1, poor (non-segmentable); 2, fair (difficult to segment); 3, acceptable (segmentation achievable by experienced reporter); 4, good (segmentation achievable by inexperienced reporter); 5, excellent (trivial segmentation).

Edge sharpness was quantified by measuring the maximum relative gradient of pixel intensities across the border of the left ventricle (LV), as previously described (16). Edge sharpness was measured in all frames and an average used for comparison.

Quantification of signal-to-noise ratio (SNR) and velocity-to-noise ratio (VNR) in this data is non-trivial due to the uneven distribution of noise, caused by the different number of interleaves in each frame and the SENSE reconstruction used (17). Therefore, in this study the signal noise (σ_s) and velocity noise in the longitudinal velocity data (σ_v) were estimated, as previously described (16,18). Estimated SNR was then calculated by dividing the mean pixel intensity inside the LV (at the peak *E* wave)

by the σ_s , and similarly, estimated VNR was calculated by dividing the mean velocity inside the LV (at the peak *E* wave in the longitudinal velocity data) by σ_v .

Post-processing of TPM data

All images were processed using in-house plug-ins for the open-source software OsiriX (the OsiriX Foundation, Geneva, Switzerland) (19). For each data set, the inner and outer myocardial borders of the LV and RV were manually segmented using the modulus images. Bulk motion correction was performed (20), before transformation of the in-plane velocities to an internal polar coordinate system positioned at the center-of-mass of the segmented ventricle. This allowed motion to be described in terms of contraction (using radial velocities – V_r) and shortening (using longitudinal velocities – V_z), in the same way as previously described (21).

Vector field plots and color-coded maps were generated for each velocity component to allow easy visualization of the results. Additionally, graphs of the temporal evolution of regional and global myocardial motion patterns were calculated, by averaging the velocity components within the region of interest (ROI). The peak velocities in the *S* (systolic), *E* (early diastolic) and *A* (atrial systolic) waves were measured for the longitudinal and radial velocities within the entire myocardium, for comparison.

Statistical Analysis

All statistical analysis was performed using GraphPad Prism (GraphPad Software Inc., San Diego, CA). The image-scoring results are expressed as the median and range, with all other results expressed as the mean \pm standard deviation (SD). The image-based respiratory navigator was compared to the simultaneously acquired airflow data by performing a correlation. A paired t-test of the CoV values was used to compare the uniformity of k-space filling between the golden-angle and simulated conventional acquisition strategies. A non-parametric Wilcoxon rank sum test was used to compare the subjective image-scoring, and paired t-tests were used to compare the quantitative image quality values between the self-navigated and the averaged spiral TPM reconstructions. A one-way ANOVA with Bonferroni's multiple comparison test was used

to compare the quantitative image quality measures and the velocities from the conventional Cartesian TPM sequence, with those from the self-navigated spiral TPM data and the averaged spiral TPM data. The calculated myocardial velocities in the LV and RV were compared between the healthy volunteers and the PH patients from the self-navigated TPM data using unpaired t-tests.

RESULTS

TPM data was successfully acquired in all 20 volunteers and 10 patients. Using the proposed self-navigated TPM sequence it was possible to quantify longitudinal and radial *S*, *E* and *A* radial velocities in the LV and RV for all 30 subjects. In the second volunteer subgroup (N=10), the conventional Cartesian sequence allowed quantification of longitudinal and radial *S* and *E* velocities in the LV and RV in all subjects, however it was only possible to quantify the *A* velocity in five of the subjects, due to the break in data acquisition.

The acquisition time for the proposed TPM sequence was 8-9 minutes, and for the conventional Cartesian sequence was an average of 10.5 minutes (range: 6.5-17.5 minutes). In the volunteer group the average heart rate was 70 ± 12 beats per minute, and in the patient group was 79 ± 18 beats per minute. In the volunteer group the average respiratory rate was 14 ± 5 breaths per minute, and in the patient group was 16 ± 4 breaths per minute.

Assessment of Respiratory Navigator

The real-time images reconstructed from the TPM data had low SNR and some residual aliasing, due to the high undersampling factor used (see Figure 1b). However, there was a high average correlation between the image-based respiratory navigator and the simultaneously acquired airflow data in 10 volunteers (0.93 ± 0.04). Figure 2c shows an example of the navigator signal and the comparable airflow data, demonstrating the similarity.

Assessment of k-Space Filling

The average number of spiral interleaves in each cardiac bin, over all 20 volunteers, was 48 (range: 20 to 75). The average CoV for the golden-angle acquisition (1.01 ± 0.05) was significantly lower than the CoV in the simulated acquisition (1.11 ± 0.05 , $p < 0.0001$). Figure 3 shows an example of one k-space from the traditional acquisition scheme and corresponding golden-angle acquisition scheme, demonstrating the more even distribution of spiral interleaves in the golden-angle acquisition scheme.

Image Quality in Averaged versus Self-navigated Spiral TPM

Examples of image quality from the self-navigated and averaged spiral TPM reconstructions can be seen in Figure 4 for one volunteer. Table 2 shows the results from the subjective image scoring and quantitative image quality measures for all subjects (N=30), comparing the averaged and self-navigated spiral TPM images. The self-navigated images had a significantly higher subjective image score, both for the LV and the RV ($P < 0.0001$). Quantitatively, they had significantly higher edge sharpness values compared to the averaged images ($P < 0.0001$). However, the self-navigated images had a significantly lower SNR and VNR (including a significantly higher σ_s and σ_v , $P < 0.0001$), compared to the averaged images ($P < 0.0001$).

Conventional Cartesian TPM versus Spiral TPM

In the second volunteer subgroup (N=10), we assessed the myocardial velocities and image quality of the conventional Cartesian acquisition against the averaged and self-navigated spiral TPM images.

The myocardial velocities measured in the LV and RV of these volunteers can be seen in Table 3. The only significant differences were seen between the averaged spiral data and the conventional Cartesian data in terms of the radial *E* wave velocity in the LV and the radial *S* wave velocity in the RV. There was a trend for the averaged spiral data to give lower velocities than the self-navigated spiral data, although none of these differences reached significance.

Table 4 shows the image quality results in this population. The Cartesian acquisition had significantly the lowest subjective image scores. However, quantitatively the edge sharpness of the Cartesian images was not significantly different from the averaged or self-navigated spiral images. The Cartesian images had a significantly lower SNR than the averaged and the self-navigated spiral images, and a significantly lower VNR compared to the averaged images, but not the self-navigated images.

Myocardial Velocities: Volunteers versus Patients

Table 5 shows the myocardial velocities measured in the LV and RV of the volunteer and patient populations using the self-navigated spiral TPM sequence. The main difference between volunteers and patients in the LV were lower longitudinal ($P=0.0006$) and radial ($P=0.0073$) S wave velocities, and higher longitudinal ($P=0.0006$) and radial ($P=0.0013$) E wave velocities. In the RV, only longitudinal E wave ($P=0.0078$), longitudinal A wave ($P=0.0190$) and radial E wave ($P=0.0112$) velocities were statistically different in patients. *Figure 5* shows the average longitudinal and radial velocity profiles in both the LV and RV, in the volunteers and the patients.

Figure 6 shows velocity vector plots for the LV and RV in one volunteer and one patient. Of particular note is the abnormal septal motion seen in this patient, due to the abnormal hemodynamics.

DISCUSSION

We have demonstrated the feasibility of measuring myocardial motion using a free-breathing, golden-angle spiral TPM sequence, with an image-based respiratory navigator calculated from the TPM data itself. We have shown this technique to be accurate compared to a conventional Cartesian TPM acquisition. Using this technique we have shown that it is possible to detect differences in myocardial motion in the LV and RV between healthy volunteers and PH patients.

Respiratory Navigation

Respiratory-navigated TPM sequences are a proven MR method of assessing myocardial motion (1,2,22). However, use of respiratory navigators and prospective gating precludes the acquisition of data throughout the cardiac cycle. This was observed in this study when using the conventional Cartesian TPM sequence, as it was only possible to quantify A wave velocities in five out of the ten volunteers. For this reason, we implemented a respiratory self-gated sequence that was also retrospectively cardiac-gated. This sequence allowed quantification of velocities throughout the entire cardiac cycle in all subjects.

In radial and spiral sequences, the repeatedly acquired center of k-space can be used as a gating signal (6,23). This technique has proven successful for cardiac-gating, but is less robust when used for respiratory-gating. Therefore, we used an image-based respiratory-navigator, as this actually evaluates the motion of the object of interest. The necessary real-time images were heavily undersampled, which did affect the raw image quality and SNR. However, image quality was sufficient to produce a navigator signal using a combination of center-of-mass assessment and cross-correlation. Theoretically, center-of-mass evaluation should produce a superior navigator compared to cross-correlation as it is linked to the position of the heart in the thorax. However, we found a pure center-of-mass navigator was not robust and thus the center-of-mass was only used to identify expiratory frames. Subsequent cross-correlation produced a more robust and accurate signal that was used for respiratory self-navigation. The resultant navigator signal was demonstrated to have a strong correlation with the measured

respiratory flow data in 10 volunteers. More importantly, the self-navigated TPM images had significantly higher edge sharpness than the TPM images reconstructed with simple respiratory averaging. This resulted in better subjective image quality scores for both the LV and RV in the self-navigated compared to the averaged spiral TPM images. Thus, this implementation of self-navigation is a successful method of removing respiratory motion artifact.

Golden-angle Acquisition

The real-time images used for navigation could have been acquired by sampling the same interleaves in every frame. However, this would result in the final gated data being undersampled by the same factor as the real-time images (i.e. acceleration factor: ~ 4). This is undesirable as the final TPM image quality would be insufficient for accurate segmentation or analysis. Consequently, each flow-encoding couplet was acquired using a golden-angle rotation strategy, which allowed for greater coverage of k-space in the gated images. Golden-angle strategies have previously been shown to produce more uniform k-space filling when reconstructing continuously acquired data at an arbitrary temporal-resolution (8-10). Even though the final navigated k-space was not acquired continuously, we speculated that a golden-angle acquisition would provide the optimum distribution of spiral interleaves. To demonstrate this we compared our data to a simulation using a previously described rotation strategy and were able to show the superiority of the golden-angle approach. Additionally, a golden-angle acquisition allows a greater degree of flexibility in the temporal-resolution of the reconstructed real-time data, which is not achievable with a conventional acquisition strategy. A drawback of having different interleaves in each resultant gated k-space, was that temporal interpolation of missing k-space lines was difficult. This is particularly true in a golden-angle approach as no k-space lines are acquired twice. Thus, retrospective gating was implemented through simple binning, accepting that this would lead to a different number of spiral interleaves in each phase. This problem was resolved with the use of an iterative SENSE reconstruction algorithm. In this study, we chose to reconstruct to a set number of frames, with no overall undersampling in the gated images. Nevertheless,

acquisition time could be reduced by lowering the number of phases or accepting more undersampling in the gated images.

Validation Against Conventional Cartesian TPM

In a subgroup of 10 volunteers there was good agreement between the self-navigated spiral TPM sequence and the conventional Cartesian acquisition. However, there were significant differences between the respiratory averaged spiral TPM data and the conventional Cartesian acquisition. Specifically, the LV radial *E* wave and RV longitudinal *S* wave velocities were lower in the averaged spiral TPM data. This demonstrates that despite the higher VNR of the averaged spiral data, this data does not provide the best estimates of clinical parameters. This is probably due to the difficulty in segmenting the averaged spiral data (reflected in the low subjective image scores and low edge sharpness values), which may result in blood pool velocities being included in the myocardial ROI's.

Comparison of TPM data in patients and volunteers

To investigate possible uses of this sequence, we compared clinically relevant myocardial velocities in volunteers and patients with pulmonary hypertension. This group was chosen because they have significant RV abnormalities, which are difficult to assess with other MR modalities, such as tagging (24). Furthermore, this patient group often has LV motion abnormalities and they are therefore a good test of the generalizability of this technique. The RV and LV abnormalities seen in the patient group may be partly due to the significant age and gender difference compared to the volunteers, with similar results seen in previous TPM studies (25). However, poor RV diastolic function (as shown by the reduced *E* wave velocity) is a hallmark of pulmonary hypertension (26), as is better preservation of RV longitudinal function compared to radial function (as shown by similar longitudinal *S* wave velocities)(27). Furthermore, changes in LV systolic and diastolic function have been demonstrated in PH (28) and may also partly explain these findings. Thus, we have demonstrated that our spiral TPM sequence is able to show differences in clinically relevant parameters. In future clinical

studies, it would be useful to assess more than one slice, as well as assess motion in the different regions of both ventricles.

Limitations

The main limitations of this study were the long acquisition and long reconstruction times for the sequence. The acquisition time of the free-breathing TPM sequence could be reduced by allowing undersampling of the cardiac-gated TPM data, using a *one-sided* encoding scheme, or removing the oversampling.

It should be noted that the proposed sequence does not include any black blood pulses (as conventionally used in TPM (22,25)) as this would have disrupted the continuous acquisition of data necessary for this implementation.

Additionally, the reconstruction time for each TPM data set was ~1 hour. This is due to the need to iteratively reconstruct the undersampled real-time data, calculate the respiratory navigator, iteratively reconstruct the averaged, cardiac-gated, TPM data, as well as perform the iterative reconstruction for the final respiratory self-navigated, cardiac-gated, TPM data. The total reconstruction time could be reduced by not reconstructing the averaged, cardiac-gated, TPM data. The remaining reconstruction steps could be sped up with the use of a graphics processing unit (GPU) (29,30).

Conclusion

We have accurately performed image-based respiratory navigation using a continuously rotating golden-angle spiral TPM sequence. We believe that the combination of respiratory self-navigation with retrospective cardiac-gating has significant benefits for TPM. Therefore, this sequence may allow better assessment of myocardial motion in patients with cardiovascular disease.

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REFERENCES

1. Delfino JG, Bhasin M, Cole R, Eisner RL, Merlino J, Leon AR, Oshinski JN. Comparison of myocardial velocities obtained with magnetic resonance phase velocity mapping and tissue doppler imaging in normal subjects and patients with left ventricular dyssynchrony. *JMRI* 2006;24(2):304-311.
2. Föll D, Jung B, Staehle F, Schilli E, Bode C, Hennig J, Markl M. Visualization of multidirectional regional left ventricular dynamics by high-temporal-resolution tissue phase mapping. *JMRI* 2009;29(5):1043-1052.
3. Jung B, Föll D, Böttler P, Petersen S, Hennig J, Markl M. Detailed analysis of myocardial motion in volunteers and patients using high-temporal-resolution MR tissue phase mapping. *Journal of Magnetic Resonance Imaging* 2006;24(5):1033-1039.
4. Thesen S, Heid O, Mueller E, Schad LR. Prospective acquisition correction for head motion with image-based tracking for real-time fMRI. *MRM* 2000;44(3):457-465.
5. Kellman P, Ched'hotel C, Lorenz CH, Mancini C, Arai AE, McVeigh ER. Fully automatic, retrospective enhancement of real-time acquired cardiac cine MR images using image-based navigators and respiratory motion-corrected averaging. *MRM* 2008;59(4):771-778.
6. Larson AC, Kellman P, Arai A, Hirsch GA, McVeigh E, Li D, Simonetti OP. Preliminary investigation of respiratory self-gating for free-breathing segmented cine MRI. *MRM* 2005;53(1):159-168.
7. Pruessmann KP, Weiger Mk, Bornert P, Boesiger P. Advances in sensitivity encoding with arbitrary k-space trajectories. *MRM* 2001;46(4):638-651.
8. Winkelmann S, Schaeffter T, Koehler T, Eggers H, Doessel O. An Optimal Radial Profile Order Based on the Golden Ratio for Time-Resolved MRI. *Medical Imaging, IEEE Transactions on* 2007;26(1):68-76.

9. Kim Y-C, Narayanan SS, Nayak KS. Flexible retrospective selection of temporal resolution in real-time speech MRI using a golden-ratio spiral view order. *MRM* 2011;65(5):1365-1371.
10. Hansen MS, Sørensen TS, Arai AE, Kellman P. Retrospective reconstruction of high temporal resolution cine images from real-time MRI using iterative motion correction. *MRM* 2011:n/a-n/a.
11. Hargreaves BA, Nishimura DG, Conolly SM. Time-optimal multidimensional gradient waveform design for rapid imaging. *MRM* 2004;51(1):81-92.
12. Bernstein MA, Shimakawa A, Pelc NJ. Minimizing TE in moment-nulled or flow-encoded two-and three-dimensional gradient-echo imaging. *JMRI* 1992;2(5):583-588.
13. Pintelon R, Schoukens J. Real-time integration and differentiation of analog signals by means of digital filtering. 1990 13-15 Feb 1990. p 346-352.
14. Lenz GW, Haacke EM, White RD. Retrospective cardiac gating: A review of technical aspects and future directions. *MRI* 1989;7(5):445-455.
15. Steeden JA, Atkinson D, Taylor AM, Muthurangu V. Assessing vascular response to exercise using a combination of real-time spiral phase contrast MR and noninvasive blood pressure measurements. *Journal of Magnetic Resonance Imaging* 2010;31(4):997-1003.
16. Steeden JA, Atkinson D, Hansen MS, Taylor AM, Muthurangu V. Rapid Flow Assessment of Congenital Heart Disease with High-Spatiotemporal-Resolution Gated Spiral Phase-Contrast MR Imaging. *Radiology* 2011;260(1):79-87.
17. Dietrich O, Raya JG, Reeder SB, Reiser MF, Schoenberg SO. Measurement of signal-to-noise ratios in MR images: Influence of multichannel coils, parallel imaging, and reconstruction filters. *JMRI* 2007;26(2):375-385.
18. Nielsen J-F, Nayak KS. Referenceless phase velocity mapping using balanced SSFP. *MRM* 2009;61(5):1096-1102.
19. Rosset A, Spadola L, Ratib O. OsiriX: An Open-Source Software for Navigating in Multidimensional DICOM Images. *Journal of Digital Imaging* 2004;17(3):205-216.
20. Hennig J, Schneider B, Peschl S, Markl M, Laubenberger TKJ. Analysis of myocardial motion based on velocity measurements with a black blood prepared

- segmented gradient-echo sequence: Methodology and applications to normal volunteers and patients. *JMRI* 1998;8(4):868-877.
21. Jung B, Markl M, Föll D, Hennig J. Investigating myocardial motion by MRI using tissue phase mapping. *European Journal of Cardio-Thoracic Surgery* 2006;29(Supplement 1):S150-S157.
 22. Petersen SE, Jung BA, Wiesmann F, Selvanayagam JB, Francis JM, Hennig J, Neubauer S, Robson MD. Myocardial Tissue Phase Mapping with Cine Phase-Contrast MR Imaging: Regional Wall Motion Analysis in Healthy Volunteers1. *Radiology* 2006;238(3):816-826.
 23. Stehning C, Börnert P, Nehrke K, Eggers H, Stuber M. Free-breathing whole-heart coronary MRA with 3D radial SSFP and self-navigated image reconstruction. *MRM* 2005;54(2):476-480.
 24. Ibrahim E-S. Myocardial tagging by Cardiovascular Magnetic Resonance: evolution of techniques--pulse sequences, analysis algorithms, and applications. *Journal of Cardiovascular Magnetic Resonance* 2011;13(1):1-40.
 25. Föll D, Jung B, Germann E, Hennig J, Bode C, Markl M. Magnetic resonance tissue phase mapping: Analysis of age-related and pathologically altered left ventricular radial and long-axis dyssynchrony. *Journal of Magnetic Resonance Imaging* 2011;34(3):518-525.
 26. Gan CT, Holverda S, Marcus JT, Paulus WJ, Marques KM, Bronzwaer JG, Twisk JW, Boonstra A, Postmus PE, Vonk-Noordegraaf A. Right ventricular diastolic dysfunction and the acute effects of sildenafil in pulmonary hypertension patients. *Chest* 2007;132(1):11-17.
 27. Kind T, Marcus JT, Westerhof N, Vonk-Noordegraaf A. Longitudinal and transverse movements of the right ventricle: both are important in pulmonary arterial hypertension. *Chest* 2011;140(2):556-557; author reply 557-558.
 28. van Wolferen SA, Marcus JT, Boonstra A, Marques KMJ, Bronzwaer JGF, Spreeuwenberg MD, Postmus PE, Vonk-Noordegraaf A. Prognostic value of right ventricular mass, volume, and function in idiopathic pulmonary arterial hypertension. *European Heart Journal* 2007;28(10):1250-1257.

29. Kowalik GT, Steeden JA, Pandya B, Odille F, Atkinson D, Taylor A, Muthurangu V. Real-time flow with fast GPU reconstruction for continuous assessment of cardiac output. *Journal of Magnetic Resonance Imaging* 2012;n/a-n/a.
30. Sorensen TS, Atkinson D, Schaeffter T, Hansen MS. Real-Time Reconstruction of Sensitivity Encoded Radial Magnetic Resonance Imaging Using a Graphics Processing Unit. *Medical Imaging, IEEE Transactions on* 2009;28(12):1974-1985.

Table 1: Imaging Parameters

	Cartesian TPM sequence	Spiral TPM sequence
TE/TR (ms)	4.24 / 6.8	3.85 / 13.60
Matrix Size	288	384
FOV (mm)	340	450
Slice Thickness (mm)	7	7
Flip Angle	25°	25°
Pixel bandwidth (Hz/pixel)	413	930
VENC X/Y/Z (cm/s)	30 / 30 / 30	30 / 30 / 30
No. of cardiac phases	17-35 Prospective (average: 25.2)	40 Retrospective
Respiratory Navigator Efficiency (%)	~34 (range: 20-59)	30
Total Scan Duration	6.5-17.5 minutes (average: 10.5)	8-9 minutes
Temporal resolution (ms)	27.12	27.14
Spatial resolution (mm)	1.18 x 1.18	1.17 x 1.17

Table 2: Image Quality – subjective image scores and quantitative measures of estimated SNR, VNR and edge sharpness for the spiral TPM sequences, for all 20 volunteers and 10 patients

	Averaged Spiral TPM	Self- Navigated Spiral TPM	P-value
Subjective Scoring			
LV	2.8 (1 to 5)	3.6 (2 to 5)*	<0.0001
RV	2.3 (1 to 4)	3.3 (1 to 4)*	<0.0001
Quantitative SNR, VNR & edge sharpness			
Estimated signal variation: σ_s	4.8 ± 1.4	$7.9 \pm 1.9^*$	<0.0001
Estimated SNR	22.4 ± 7.9	$14.1 \pm 3.3^*$	<0.0001
Estimated velocity variation: σ_v (cm/s)	1.6 ± 0.5	$3.0 \pm 1.0^*$	<0.0001
Estimated VNR	8.1 ± 4.5	$4.6 \pm 2.2^*$	<0.0001
Edge Sharpness (mm^{-1})	0.12 ± 0.04	$0.17 \pm 0.04^*$	<0.0001

* Self-navigated value is significantly different from averaged value

Table 3: Tissue phase mapping velocity results comparing the conventional Cartesian acquisition to the averaged and navigated spiral acquisition in the volunteer subgroup (N=10)

Velocity (cm/s)	Conventional Cartesian TPM	Averaged Spiral TPM	Self-Navigated Spiral TPM
LV			
Longitudinal, S	5.07 ± 1.09	4.92 ± 0.94	4.96 ± 1.12
Longitudinal, E	-6.33 ± 1.58	-6.28 ± 1.73	-6.44 ± 1.76
Longitudinal, A	-	-2.57 ± 0.84	-2.67 ± 0.76
Radial, S	2.67 ± 0.26	2.58 ± 0.36	2.61 ± 0.30
Radial, E	-3.99 ± 0.69	-3.73 ± 0.67 *	-3.84 ± 0.72
Radial, A	-	-1.64 ± 0.39	-1.64 ± 0.35
RV			
Longitudinal, S	3.8 ± 1.1	3.4 ± 1.0*	3.8 ± 1.1
Longitudinal, E	-4.0 ± 1.6	-3.9 ± 1.5	-3.9 ± 1.4
Longitudinal, A	-	-3.2 ± 1.5	-3.1 ± 1.6
Radial, S	1.9 ± 0.6	1.8 ± 0.6	1.9 ± 0.6
Radial, E	-3.1 ± 1.6	-2.6 ± 1.5	-2.8 ± 1.5
Radial, A	-	-1.4 ± 0.8	-1.3 ± 1.0
* Velocity is significantly different from Cartesian TPM (P<0.05)			
^ Velocity is significantly different from averaged spiral TPM (P<0.05)			

Table 4: Image Quality – subjective image scores and quantitative measures of estimated SNR, VNR and edge sharpness for the conventional Cartesian sequence and the spiral TPM sequences, for a the seconds subgroup of volunteers (N=10)

	Conventional Cartesian TPM	Averaged Spiral TPM	Self- Navigated Spiral TPM
Subjective Scoring			
LV	2.7 (2 to 3)	3.2 (2 to 4)*	3.9 (3 to 5)*^
RV	2.2 (1 to 3)	3.0 (2 to 4)*	3.6 (3 to 4)*^
Quantitative SNR, VNR & edge sharpness			
Estimated signal variation: σ_s	7.1 \pm 2.0	4.8 \pm 1.7*	8.7 \pm 2.8^
Estimated SNR	8.1 \pm 3.0	23.9 \pm 8.3*	13.1 \pm 3.3*^
Estimated velocity variation: σ_v (cm/s)	4.8 \pm 1.0	1.7 \pm 0.5*	3.4 \pm 1.0*^
Estimated VNR	3.2 \pm 1.4	9.3 \pm 4.3*	4.8 \pm 2.3^
Edge Sharpness (mm ⁻¹)	0.18 \pm 0.02	0.17 \pm 0.03	0.20 \pm 0.03^

* Value is significantly different from conventional Cartesian TPM value (P<0.05)

^ Value is significantly different from averaged spiral TPM value (P<0.05)

Table 5: Tissue phase mapping velocity results in the volunteer population (N=20) and patient population (N=10), measured using the self-navigated spiral TPM sequence

Velocity (cm/s)	Volunteer Population	Patient Population	P-value
LV			
Longitudinal, S	5.2 ± 1.1	3.5 ± 1.1*	0.0006
Longitudinal, E	-6.7 ± 2.1	-3.4 ± 2.5*	0.0006
Longitudinal, A	-2.6 ± 1.0	-3.1 ± 1.6	0.4032
Radial, S	2.6 ± 0.3	2.2 ± 0.4*	0.0073
Radial, E	-3.7 ± 0.8	-2.5 ± 1.2*	0.0013
Radial, A	-1.6 ± 0.5	-1.8 ± 0.6	0.3436
RV			
Longitudinal, S	4.1 ± 1.2	4.4 ± 1.1	0.6236
Longitudinal, E	-4.5 ± 1.5	-2.7 ± 1.6*	0.0078
Longitudinal, A	-3.16 ± 1.8	-5.7 ± 2.8*	0.0190
Radial, S	2.1 ± 0.7	1.8 ± 0.5	0.2313
Radial, E	-2.6 ± 1.6	-1.1 ± 0.9*	0.0112
Radial, A	-1.3 ± 0.8	-1.8 ± 0.7	0.1523

* Velocity for patient population is significantly different from volunteer population

Figure Legends:

Figure 1: Golden-angle acquisition strategy. a) Continuous golden-angle acquisition, with golden-angle rotation factor shown by numerical values. Colours represent different flow-encoding couplet directions; X shown in red, Y shown in blue and Z shown in green. Ten consecutive flow-encoding couplets are combined into one k-space to make each real-time frame. b) Example of the real-time image quality from one frame in a volunteer.

Figure 2: Image-based respiratory self-navigation. a) Calculation of image-based respiratory navigator from cross-correlation of all real-time images, with five frames known to be in expiration (from center-of-mass). b) Final image-based respiratory navigator displayed on top of a projection image of the real-time data. c) Correlation of image-based respiratory navigator (red) with measured airflow (blue).

Figure 3: k-Space filling from simulated conventional acquisition strategy and golden-angle acquisition strategy, for one respiratory-navigated, cardiac binned frame in one volunteer.

Figure 4: Example of image quality from one volunteer, for the conventional Cartesian TPM data, the averaged spiral reconstruction and for the respiratory self-navigated spiral reconstruction.

Figure 5: Average velocity profiles in the LV and RV, for healthy volunteers (N=20) and patients (N=10). The error bars show the standard deviation.

Figure 6: Example velocity vector plots shown in the LV and RV from one volunteer and one patient. The vector colors represent the longitudinal velocities, with reds representing myocardial motion towards the apex, and blues representing myocardial motion away from the apex.