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A novel super-resolution approach to time-resolved volumetric 4DMRI with high spatiotemporal resolution for multi-breathing cycle motion assessment

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Abstract

Purpose—To develop and evaluate a super-resolution approach to reconstruct time-resolved four-dimensional magnetic resonance imaging (TR-4DMRI) with a high spatiotemporal resolution for multi-breathing cycle motion assessment.

Methods and Materials—A super-resolution approach was developed to combine fast 3D cine MRI with low-resolution during free breathing (FB) and high-resolution 3D static MRI during breath hold (BH) using deformable image registration (DIR). A T1-weighted, turbo field echo sequence, coronal 3D cine acquisition, partial Fourier approximation, and SENSE parallel acceleration were employed. The same MRI pulse sequence, field of view, and acceleration techniques were applied in both FB and BH acquisitions; the intensity-based Demons DIR method was used. Under an IRB-approved protocol, seven volunteers were studied with 3D cine FB scan (voxel size: 5x5x5mm³) at 2Hz for 40s and a 3D static BH scan (2x2x2mm³). To examine the image fidelity of 3D cine and super-resolution TR-4DMRI, a mobile gel phantom with multi-internal targets was scanned at three velocities and compared with the 3D static image. Image similarity among 3D cine, 4DMRI, and 3D static was evaluated visually using difference image and quantitatively using voxel intensity correlation and Dice index (phantom only). Multi-breathing-cycle waveforms were extracted and compared in both phantom and volunteer images using the 3D cine as the references.

Results—Mild imaging artifacts were found in the 3D cine and TR-4DMRI of the mobile gel phantom with a Dice index of >0.95. Among seven volunteers, the super-resolution TR-4DMRI yielded high voxel-intensity correlation (0.92±0.05) and low voxel-intensity difference (<0.05).

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The detected motion differences between TR-4DMRI and 3D cine were -0.2 ± 0.5 mm (phantom) and -0.2 ± 1.9 mm (diaphragms).

Conclusion—Super-resolution TR-4DMRI has been reconstructed with adequate temporal (2Hz) and spatial ($2 \times 2 \times 2$ mm³) resolutions. Further TR-4DMRI characterization and improvement are necessary before clinical applications. Multi-breathing cycles can be examined, providing patient-specific breathing irregularities and motion statistics for future 4D radiotherapy.

Keywords

Respiratory motion simulation; Magnetic resonance imaging; Image reconstruction; Treatment planning; and Motion artifacts

Introduction

Volumetric four-dimensional magnetic resonance imaging (4DMRI) techniques have been under investigation over the past decade (1–5), aiming to provide a new 4D imaging modality with high soft-tissue contrast, no ionizing radiation, and possible multi-breathing cycles for 4D radiotherapy planning (5–7). Non-volumetric cine methods with orthogonal 2D cine images are inadequate for delineating tumor volume and organ motion (8–10). Initially, dynamic volumetric 4DMRI, or time-resolved (TR) 4DMRI, was achieved by capturing a series of 3D MRI images with a 1Hz frame rate and compromised image resolution using parallel imaging and k-space approximation (1). Due to the physical limit of MR relaxation, acquisition speed has become a limiting factor for 4D acquisition. Hence, investigations have shifted to respiratory-correlated (RC) 4DMRI using internal respiratory surrogates and choice of non-axial scanning directions (2, 4, 11) for 4DMRI reconstruction. Like 4D computed tomography (4DCT) (12, 13), RC-4DMRI produces a composite single-breath 4D image with binning artifacts caused by common breathing irregularities that violate the assumed periodic motion(11).

To overcome these limitations, TR-4DMRI has recently been revisited to capture irregular organ motions and produce multi-breath volumetric images. Using principal component analysis (PCA) and deformable image registration (DIR), similar to reported cone-beam CT methods (14, 15), Harris, et al. (16) built an *a priori* motion model with three extracted deformation patterns from RC-4DMRI to match orthogonal 2D cine images to reconstruct TR-4DMRI images of the thorax. Similarly, Stemkens, et al. (17) used the PCA-DIR method to extract two PCA components from RC-4DMRI and deformed the model to match 2D cine images to achieve abdominal TR-4DMRI. However, because RC-4DMRI carries binning artifacts, PCA is an approximation method, and 2D cine may exceed the deformation range of the respiratory model, these uncertainties would propagate into the TR-4DMRI images.

The super-resolution approach, which combines two insufficient image datasets with complementary strengths to produce a super-resolution image, has been proven effective to overcome resolution limitations of a given imaging modality (18). In MRI and CT imaging, the super-resolution concept has been applied to improve image quality. Dowsey, et al. used super-resolution with the COMB tag tracking technique to perform motion compensation (19). Van Reeth, et al. reported an isotropic voxel image utilizing multiple anisotropic voxel

images (20). Miguel, et al. studied a patient-specific respiratory model based on combined images from various respiratory cine and static images using B-Spline registration (21). Wu, et al. applied super-resolution to estimate lung motion using spatiotemporal images and produce 4DCT using the 3DCT of the day (22). Super-resolution has become an effective approach to overcome imaging detection limits and produce superior image quality.

In this study, we developed a super-resolution approach to reconstruct TR-4DMRI with a clinically acceptable spatiotemporal resolution for multi-breath motion assessment. Two MRI image sets were acquired using the same pulse sequence, field of view (FOV), scanning orientation, and acceleration techniques, including a 3D cine series (2Hz) at low spatial resolution during free breathing (FB) and a 3D static image at high spatial resolution during breath hold (BH). A Demons-based DIR technique was applied to map the high spatial resolution from BH to FB images. Using a mobile gel phantom the image fidelity of 3D cine and super-resolution TR-4DMRI images were examined. Seven volunteers were studied under an IRB-approved protocol to demonstrate and evaluate the image quality of the super-resolution multi-breath TR-4DMRI.

Methods and Materials

Image acquisition of 3D cine FB and 3D static BH images

An IRB-approved protocol was established and seven volunteers were scanned with 3D cine FB (2Hz and $5 \times 5 \times 5 \text{ mm}^3$ voxel size) for about 40s, followed by a 3D static BH scan ($2 \times 2 \times 2 \text{ mm}^3$) at an arbitrary respiratory phase within 20s using a 3T MRI scanner (Ingenia, Philips Healthcare, The Netherlands). A T1W, multi-shot, turbo field echo (TFE) sequence was employed with TE/TR of 1.9ms/4.2ms and a flip angle of 15° . The readout direction was in the superior-to-inferior (SI) direction, the slice encoding was in the anterior-to-posterior (AP) direction, and the phase encoding was in right-to-left (RL) direction. Parallel imaging with SENSE factors of 4 (RL) and 2 (AP) was applied for 3D cine acquisition, whereas SENSE factors of 2.5 (RL) and 1.5 (AP) were applied for 3D static acquisition. Partial Fourier approximation (a factor of 0.8) (23) and central-to-peripheral k-space acquisition order (CENTRA) (24) were employed for further acceleration with preserved temporal anatomic integrity, respectively. The same FOV covering from the thorax to the upper abdomen were used for both 3D cine FB and 3D static BH acquisitions.

A super-resolution method using deformable image registration (DIR)

The super-resolution concept (18) was applied to reconstruct a TR-4DMRI image with an adequate spatiotemporal resolution using a Demons-based DIR algorithm to map the high-resolution 3D static image to the low-resolution 3D cine images. Figure 1 illustrates the schematic of the super-resolution approach to reconstruct the TR-4DMRI using DIR.

A modified Demons algorithm (25, 26) was implemented in MatLab. The image gradients from moving image ($\vec{V}_m$) and static image ($\vec{V}_s$) were used as the driving forces to move the voxels and minimize the gradient while applying a Gaussian filter to “diffuse” the nearby voxels, and thereby achieving a match of their common underlying anatomy through an

iterative optimization process. The total force field with a normalization factor (α) can be expressed in the optical flow equation:

$$\vec{f} = (m-s) \times \left(\frac{\vec{\nabla}_m}{|\vec{\nabla}_m|^2 + \alpha^2(m-s)^2} + \frac{\vec{\nabla}_s}{|\vec{\nabla}_s|^2 + \alpha^2(m-s)^2} \right) \quad (1)$$

where m and s denote the moving and static images, respectively. This modified Demons was implemented with a two-level multi-resolution approach ($\alpha=0.4$ at low resolution and 0.7 at high resolution). The mean voxel intensity difference (VID) within a region of interest (ROI) was employed as the metric for minimization and stopping criterion ($\text{VID} < 0.01$). The ROI was a user-defined 3D box covering about 10 cm on each side of the diaphragm within the body. The final mean voxel-intensity correlation (VIC) and VID on the entire image were reported.

Image fidelity of 3D cine and TR-4DMRI in mobile phantom experiments

High image fidelity of 3D cine images is essential because they served as the templates for DIR to map high resolution from the 3D static image. To assess image fidelity, a gel phantom was built in a glass beaker (1 liter) containing several internal “target” objects with known geometric sizes and shapes. A mobile platform was used to carry the phantom to move in three sinusoidal waveforms with motion range (period) of 2cm (4s), 2cm (3s) and 4cm (4s), similar to the human respiratory motion. The same 4DMRI scan protocol (pulse sequence, FOV, scan direction, and acceleration) used in human subjects was applied in the mobile phantom experiments to acquire 3D cine and 3D static images.

The 3D cine images of the phantom acquired at the highest speed ($V_{max} = \pi \cdot \frac{\text{Range}}{\text{Period}} = \frac{\pi}{2} \bar{v}$) were used to compare with the 3D static image. The image quality of super-resolution TR-4DMRI was evaluated after both rigid alignment and DIR were evaluated using VID, VIC, and the Dice index of the segmented phantom (described next). The phantom motion trajectories from the 3D cine and TR-4DMRI images were extracted using the center of mass (COM) of the phantom as a function of time and compared with statistical analysis using 3D cine as references.

Three image similarity measures used in this study

Three image similarity measures were applied to assess the DIR results, in addition to visual verification with difference images. The mean VIC was defined as:

$$\text{VIC} = \bar{\rho}\{I_m, I_s\} = \frac{\text{cov}(I_m, I_s)}{\sigma_{I_m} \cdot \sigma_{I_s}} \quad (2)$$

where the I_m and I_s denote the voxel intensity of the moving and static images, respectively. The cov is the covariance and σ is the standard deviation. The VID in a difference image with a total number of N voxels was defined as:

$$VID = \frac{1}{N} \sum_i^N |I_m - I_s| \quad (3)$$

The Dice index was applied to compare image fidelity based on segmented phantom images. Between the moving (C_m) and static (C_s) images, the Dice index was expressed as:

$$Dice = \frac{2|C_m \cap C_s|}{|C_m| + |C_s|} \quad (4)$$

Super-resolution TR-4DMRI images of human subjects

In volunteer subjects, the image similarity among 3D cine, 3D static, and TR-4DMRI was analyzed and evaluated using Eqs. 2 and 3, difference images, and point tracking comparison. Before DIR, the 3D cine FB images were interpolated to have the same image matrix size as the 3D static BH image. TR-4DMRI reconstruction was performed automatically for all 77–81 volumetric images in the 3D cine series (~40s over 6–13 breathing cycles), and the results were saved as new DICOM images, displacement vector fields (DVs), and optimization parameters.

The anatomic alignment of volunteer anatomy was checked visually using difference images. Quantitatively, the motion trajectories of the apex points at the right and left diaphragm domes were manually tracked in 3D cine and TR-4DMRI using ImageJ(27). The origin of each motion trajectory was set to their median displacement and the precision of this manual process was limited by the voxel size (<2mm). As in one subject both full-inhalation and full-exhalation BH images were acquired (diaphragm displacement of 3.4cm), we performed DIR from BH-E to a simulated 3D cine by reducing the resolution of the BH-I image, and compared the deformed image with the original BH-I as the ground truth, and vice versa. Three liver vessel bifurcation points and a unique point in the abdomen were used for alignment evaluation in the low contrast regions.

Inverse consistency error (ICE) in TR-4DMRI images of human subjects

The ICE is a common way to evaluate DIR consistency in the absence of absolute truth (28) and it is defined based on the net DVFs between forwarding DVF (DVF_f) and backward DVF (DVF_b) as the following:

$$ICE = |DVF_f \circ DVF_b| \quad (5)$$

where the composite operator $\circ$ between the two DVFs. We only evaluated one direction from high resolution to low resolution as used in the TR-4DMRI image reconstruction.

Results

Image fidelity of 3D cine scan based on mobile phantom experiments

A visual comparison between 3D cine and 3D static images of the phantom is shown in Figures 2A and 2B. Mild image blurring, shape distortion, and ring artifacts were observed in 3D cine images. As the maximum motion speed increases from 1.6 to 3.1 cm/s, the severity of imaging artifact increases slightly. The difference images (Figure 2C) show minor difference, mostly resulting from different image resolutions. Table I tabulates the VIC (0.98 ± 0.01), VID (0.028 ± 0.001), and the Dice index (0.96 ± 0.02) of the segmented gel phantom between 3D cine and 3D static images. All three measures indicate high image fidelity of 3D cine imaging, suggesting that the 3D cine images can serve as references for validating the TR-4DMRI.

Geometric feature preservation by the super-resolution 4DMRI method

The super-resolution 4DMRI images of the mobile phantom were compared with the static image, showing negligible difference in VIC and VID. Figures 2C (rigid registration) and 2D (deformable registration) are similar. The smallest objects ($\phi \approx 5\text{mm}$) in Figure 2A are severely blurred at the highest speed but are preserved in the TR-4DMRI image. Table I tabulates VIC (0.98 ± 0.01), VID (0.027 ± 0.001), and Dice similarity coefficient (0.95 ± 0.02) between the TR-4DMRI and the 3D static images. The high image similarity suggests that 3D cine image fidelity is sufficient to serve as templates to reconstruct high-quality TR-4DMRI images.

Super-resolution TR-4DMRI images of volunteers and diaphragm motion trajectory

The super-resolution TR-4DMRI images of three volunteers are illustrated in Figure 3. The diaphragm alignments are achieved with high VIC and low VID. Table II summarizes the DIR quality of the super-resolution TR-4DMRI images for all seven volunteers, including the VIC (0.90 ± 0.02), VID (0.054 ± 0.003), tracked-point motion difference ($-0.2 \pm 1.9\text{mm}$), ICE ($0.8 \pm 3.6\text{mm}$) and DIR performance ($8.1 \pm 4.8\text{ min}$). The maximum diaphragm displacement between FB and BH is $22 \pm 5\text{mm}$, ranging 16–30mm. For the simulated DIR validation using two extreme BH images, the discrepancy between four corresponding points in the low-contrast abdominal region is about 5mm, which should be the upper limit of the DIR uncertainty since the diaphragm displacement is 34mm, greater than the deformation range in TR-4DMRI reconstruction.

Figure 4 shows the motion trajectories of extracted points from the 3D cine and super-resolution TR-4DMRI images of the mobile phantom (COM) and three volunteers (the apex points of the diaphragm domes). The COM trajectories of the mobile phantom have sub-mm errors: $-0.1 \pm 0.4\text{mm}$, $-0.4 \pm 0.5\text{mm}$, and $-0.2 \pm 0.5\text{mm}$. A higher motion difference ($-0.2 \pm 1.9\text{mm}$) is observed in the motion trajectories because of the uncertainty in single point tracking and 2mm voxel sizes. Table II tabulates the motion difference in all seven volunteers. The consistency between 3D cine and TR-4DMRI demonstrates the upper limit of the DIR uncertainty because the diaphragm has the largest deformation.

Discussion

The super-resolution approach to TR-4DMRI with adequate spatiotemporal resolution

Time-resolved 4DMRI is the most desirable technique for clinical applications if an adequate spatiotemporal resolution can be provided because it can capture any motions (cyclical or noncyclical) without the need of a motion surrogate. Using existing acceleration and approximation techniques, a 3D cine image with a spatiotemporal resolution of $5 \times 5 \times 5 \text{ mm}^3$ and 2Hz cannot meet clinical needs. Therefore we have developed the super-resolution approach to overcome the scan speed limits, providing sufficient spatiotemporal resolution ($2 \times 2 \times 2 \text{ mm}^3$ and 2Hz). The super-resolution concept has been proven effective to overcome the resolution limit of an imaging technique (18) by applying an independent data-processing technique to combine two image sets with different strengths. In this study, we applied a Demons-based DIR to combine a high spatial-resolution 3D static BH image ($2 \times 2 \times 2 \text{ mm}^3$) with a high temporal-resolution 3D cine FB to achieve TR-4DMRI over multi-breathing cycles, allowing for assessment of breathing irregularities in 4D planning.

As DIR is used as the principal technique in the super-resolution approach, its reliability and accuracy are of crucial importance. We employed the Demons-based DIR algorithm (25, 26, 29–31) and conducted DIR validation in the context of TR-4DMRI reconstruction using a mobile phantom and volunteer experiments by tracking the alignment of corresponding points with respect to the 3D cine images. Both quantitative and visual assessments (Table I and Figures 2–4) demonstrate high image fidelity of the 3D cine and TR-4DMRI.

Reliability of the 3D cine images as the template for DIR mapping

The image fidelity of the 3D cine scans is essential to produce an accurate, reliable super-resolution TR-4DMRI. In the image acquisition, we also tried the sequence of balanced steady-state free precession (bSSFP) in 3D cine scans; however, the banding artifacts (dark bands) around the tissue-air interfaces may occur and cannot serve as reliable templates to produce high-fidelity super-resolution TR-4DMRI. Therefore, we used a faster T1W sequence, which has minimal known motion-related artifacts, together with the CENTRA method and lateral phase encoding for further minimizing motion artifacts. As shown in the mobile phantom results (Table I and Figures 2–4), T1W 3D cine image fidelity is high, sufficient to reconstruct high-fidelity TR-4DMRI. A sub-mm uncertainty ($-0.2 \pm 0.5 \text{ mm}$) was observed in COM-tracked trajectory. In the volunteer study, it is clear that the precision of the manually tracked points is limited by the voxel size of the images (Figure 4), even with a finer interpolated voxel (2 mm) for 3D cine images. The observed uncertainty ($-0.2 \pm 1.9 \text{ mm}$) at the extracted diaphragm may serve as an indicator for TR-4DMRI uncertainty. Additionally, we have provided averaged ICE results for 7–14 extreme respiratory states ($0.8 \pm 3.6 \text{ mm}$), which is similar to the uncertainty at the diaphragm interface. Further validation of this technique is currently under investigation.

Advantages of TR-4DMRI in comparison with RC-4DMRI

The hallmark of the super-resolution TR-4DMRI is the independent, video-like volumetric imaging with adequate spatiotemporal resolution. It is capable of imaging irregular motions, and therefore will not be affected by breathing irregularities, “random” digestive/cardiac

motions, or patient voluntary body motions. Compared with the model-based, 2D cine-guided TR-4DMRI (16, 17), which incorporates RC-4DMRI with binning artifacts, PCA-DIR approximation, possible extrapolation, and lacks confirmation (outside of orthogonal 2D planes), this super-resolution TR-4DMRI technique offers a superior edge as an independent 4D imaging modality with reduced uncertainties and volumetric verification using 3D cine as references.

The 2Hz frame rate of TR-4DMRI produces ~8 frames per breathing cycle (~4s), similar to RC-4DMRI and 4DCT, where 10 bins are commonly used. Motion irregularity assessment, possible only when multi-breathing cycle imaging is available, such as TR-4DMRI, is important for 4D treatment planning and critical for dose-accelerated hypofractionated stereotactic treatments (7), as there is little leverage from statistical averaging, unlike conventional multi-fraction treatments.

Second, as the super-resolution TR-4DMRI does not assume periodic motion and does not need a respiratory surrogate, it eliminates binning artifacts, unlike RC-4DMRI, or 4DCT (12, 13). Owing to the binning artifacts in 4DCT, delineated gross tumor volumes can vary as much as 90–110% among the single-breathing-cycle images (32, 33). On the contrary, TR-4DMRI may offer more accurate tumor/organ delineation, although a further clinical study is necessary to prove this expectation. In addition, this 3D cine-guided TR-4DMRI technique is an independent volumetric 4D imaging approach, whereas the 2D cine-guided TR-4DMRI method depends on RC-4DMRI (16, 17) results.

Lastly, using the TR-4DMRI technique patient-specific organ motions can be captured and characterized without *a priori* knowledge, and the 3D cine data set provides a dynamic ground truth although low-resolution. This volumetric motion image is useful to build and validate an organ motion model. A respiratory motion model was studied based on dynamic MRI images derived from FB and BH by B-Spline non-rigid registration (21), despite the fact that bSSFP sequence was used, which may often contain banding artifacts. In contrast, the T1W-based TR-4DMRI technique has high image fidelity and is useful in assessing the accuracy of a physical perturbation motion model (34) and internal-external motion relationship (11). Using RC-4DMRI or 4DCT to build a patient-specific motion model has been reported for different clinical applications (14–17, 34, 35). However, RC 4D imaging may suffer from severe binning artifacts (7, 12, 13) and limited motion statistics (7), unlike the TR-4DMRI approach.

Limitations and future directions

Currently, the imaging frame rate for 3D cine is limited to 2Hz, and we are investigating the use of a compressed sensing technique (36) to further accelerate 3D cine acquisition. Also, the MRI scanner has a computer memory limit; only ~40s of 3D cine images (77–81 image volumes) can be captured within a single acquisition with ~100 MB image data. Gaps among multiple acquisitions are inevitable for a longer series of TR-4DMRI.

Although the Demons-based DIR algorithm works fairly well, it still has some shortcomings, including limited deformation ranges, uncertainty in handling sliding motion at the chest wall, expected inferior DIR accuracy at low soft-tissue contrast, and relatively

slow performance. The accuracy in high-contrast regions, such as at the diaphragm-lung interface, may not be directly applied to low-contrast regions, such as inside the liver. In fact, the upper limit of uncertainty could be 4–6mm, and further improvement is necessary for clinical application. The DIR speed can be improved by using GPU to reduce DIR time from several minutes to several seconds (29–31). In this study, the largest diaphragm displacement between FB and BH is 3cm; whether the DIR method can accommodate >3cm deformation needs further investigation. We are now investigating solutions to enhance the dynamic range and performance in reconstructing TR-4DMRI images.

Conclusion

A super-resolution time-resolved 4DMRI technique with a voxel size of $2 \times 2 \times 2 \text{ mm}^3$ and a frame rate of 2Hz has been established and tested in both mobile phantom and healthy volunteer experiments. The image fidelity of the fast 3D cine scan and TR-4DMRI reconstruction is high, quantified by $>0.95 \text{ VIC}$, $<0.05 \text{ VID}$, and $>0.96 \text{ Dice index}$ in a phantom study. The volunteer study depicts similar high-quality TR-4DMRI results with an uncertainty of $-0.2 \pm 1.9 \text{ mm}$ at the diaphragm. In the low contrast region, however, the uncertainty is higher and under further investigation. This super-resolution TR-4DMRI is under further evaluation in patient studies under IRB-approved clinical trials.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Summary

This study presents a super-resolution approach to achieve time-resolved 4DMRI over multi-breathing cycles with a clinically-adequate spatiotemporal resolution through deformable image registration from a high-resolution breath-hold 3D static image to low-resolution free-breathing 3D cine images. A mobile phantom and seven volunteer experiments were conducted to validate this new approach. This TR-4DMRI technique can image irregular motion without binning artifacts, show high soft-tissue contrast without radiation, and provide multi-breath motion statistics for future high-precision motion-compensated treatment planning.

Figure 1.
Schematic of the super-resolution approach to achieve multi-breath TR-4DMRI with high spatiotemporal resolution using deformable image registration.

Figure 2.

Image fidelity of the 3D cine and 4DMRI images. Three 3D cine images ($5 \times 5 \times 5 \text{ mm}^3$ and 2Hz) (A) were captured at the maximum velocity ($= \pi/2 \times \bar{v}$) in three sinusoidal motions, in reference to 3D static image (B), and the difference image (C) shows small residual errors (voxel-intensity correlation, VIC 0.96 and voxel-intensity difference, VID < 0.03). The 3D cine image quality decreases as the motion velocity increases. The difference image of 4DMRI images (D) in reference to the 3D static image (B) depicts almost identical residual errors.

Figure 3.

Examples of super-resolution TR-4DMRI images of three volunteers. (A) low-resolution 3D cine images, (B) high-resolution 3D BH images, (C) super-resolution TR-4DMRI images, (D) difference images between 3D cine and 3D static images, (E) difference images between 3D cine and TR-4DMRI images, and (F) plots of correlation as a function of coronal slices before and after DIR. The diaphragm DIR alignments were highlighted by red lines and arrows.

Figure 4.

Motion trajectories of the center of mass (COM) of the mobile phantom and the tracking points at both diaphragm domes of three volunteers based on 3D cine and TR-4DMRI images. The COM point, averaged from all points within the phantom, is more accurate than the single tracking point at the diaphragm, which is limited by the displayed image voxel sizes (1–2mm³) with interpolation.

Image fidelity of 3D cine and super-resolution TR-4DMRI images of the gel phantom on a mobile platform that moves in sinusoidal waveforms, in reference to the 3D static images. Rigid image registration was performed to align the 3D cine with 3D static image, while DIR was performed after the rigid alignment for TR-4DMRI. Three descriptors of image fidelity (voxel intensity correlation, mean intensity difference, and Dice index of the segmented phantom) are listed. The average is based on 77–81 volumes acquired during ~40 seconds for each of the motion experiments.

Table I

Exam	Motion	Range (cm)	Period (s)	$\vec{v} v_{max}^*$ (cm/s)	Correlation		Mean Diff		Dice index	
					Mean	Stdev	Mean	Stdev	Mean	Stdev
3D cine	1	2.0	4.0	1.0 (1.6)	0.98	0.01	0.029	0.001	0.96	0.02
	2	2.0	3.0	1.3 (2.0)	0.98	0.01	0.029	0.002	0.96	0.02
	3	4.0	4.0	2.0 (3.1)	0.97	0.01	0.028	0.002	0.95	0.02
Average		2.7	3.7	1.4 (2.2)	0.98	0.01	0.028	0.002	0.96	0.02
St dev					0.01	0.00	0.001	0.000	0.01	0.00
4DMRI	1	2.0	4.0	1.0 (1.6)	0.98	0.01	0.028	0.001	0.96	0.02
	2	2.0	3.0	1.3 (2.0)	0.98	0.01	0.028	0.002	0.95	0.02
	3	4.0	4.0	2.0 (3.1)	0.97	0.01	0.026	0.002	0.94	0.03
Average		2.7	3.7	1.4 (2.2)	0.98	0.01	0.027	0.001	0.95	0.02
St dev					0.01	0.00	0.001	0.000	0.01	0.00

* The mean velocity ($\vec{v}$) calculated by dividing the range with half of the period. The maximum velocity ($v_{max} = \frac{\pi}{2} \times \overline{v}$) is the mean velocity multiplied by a factor of $\pi/2 = 1.57$.

Super-resolution TR-4DMRI images of seven healthy volunteers scanned under an IRB-approved protocol. The average voxel intensity correlation, mean intensity difference, point displacement difference (at the diaphragm dome), and DIR optimization time (per image pair) are shown between 4DMRI and 3D cine. The average is taken from the 77–81 volumes over ~40s acquisition.

Table II

Subject	Deformation Range (mm)			Voxel Correlation		Mean Intensity Diff		Accuracy (mm) #		ICE & (mm)		DIR time (min)	
	Cycle range	BH pos	Net range	Ave	St. dev	Ave	St. dev	Ave	St. dev	Ave	St. dev	Ave	St. dev
1	26	1	25	0.91	0.02	0.051	0.003	-0.4	2.8	0.8	3.0	10.2	4.5
2	22	6	16	0.87	0.03	0.065	0.003	-0.1	1.2	0.8	3.6	7.2	2.3
3	18	-3	21	0.94	0.01	0.040	0.002	-0.5	1.7	0.5	2.3	40* 20*	
4	52	26	26	0.86	0.03	0.064	0.004	-0.3	2.8	1.0	5.4	9.4	8.2
5	32	13	19	0.90	0.01	0.053	0.003	0.4	1.2	0.7	3.7	5.9	2.6
6	36	19	17	0.89	0.01	0.046	0.001	-0.5	3333	0.8	3.3	9.4	333
7	36	6	30	0.89	0.01	0.057	0.004	0.2	1.7	1.0	4.0	6.3	2.8
Ave	32	10	22	0.90	0.02	0.054	0.003	-0.2	1.9	0.8	3.6	8.1	4.8
St. dev	11	10	5	0.03	0.01	0.009	0.001	0.4	0.7	0.2	1.0	1.8	2.8

#The DIR accuracy based on manual point tracking of two diaphragm domes is limited by the 5mm voxel size of 3D cine images and 2mm voxel size of 4DMRI images.

&The inverse consistency error (ICE) defined in Eq.5.

* This long DIR optimization time is due to the use of a particularly stringent stopping criterion. This data is excluded from calculating the average time.