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Accelerating Volumetric Cine MRI (VC-MRI) using Undersampling for real-time 3D Target Localization/Tracking in Radiation Therapy: A Feasibility Study

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Abstract

Purpose—To accelerate volumetric cine MRI (VC-MRI) using undersampled 2D-cine MRI to provide real-time 3D guidance for gating/target tracking in radiotherapy.

Methods—4D-MRI is acquired during patient simulation. One phase of the prior 4D-MRI is selected as the prior images, designated as MRI_{prior} . The on-board VC-MRI at each time-step is considered a deformation of the MRI_{prior} . The deformation field map (DFM) is represented as a linear combination of the motion components extracted by Principal Component Analysis (PCA) from the prior 4D-MRI. The weighting coefficients of the motion components are solved by matching the corresponding 2D-slice of the VC-MRI with the on-board undersampled 2D-cine MRI acquired. Undersampled Cartesian and radial k-space acquisition strategies were investigated. The effects of k-space sampling percentage (SP) and distribution, tumor sizes and noise on the VC-MRI estimation were studied. The VC-MRI estimation was evaluated using XCAT simulation of lung cancer patients and data from liver cancer patients. Volume Percent Difference (VPD), Center of Mass Shift (COMS) of the tumor volumes and tumor tracking errors were calculated.

Results—For XCAT, VPD/COMS were $11.93 \pm 2.37\% / 0.90 \pm 0.27\text{mm}$ and $11.53 \pm 1.47\% / 0.85 \pm 0.20\text{mm}$ among all scenarios with Cartesian sampling (SP=10%) and radial sampling (21spokes, SP=5.2%), respectively. When tumor size decreased, higher sampling rate achieved more accurate VC-MRI than lower sampling rate. VC-MRI was robust against noise levels up to SNR=20. For patient data, the tumor tracking errors in Superior-Inferior (SI), Anterior-Posterior (AP) and Lateral (LAT) directions were $0.46 \pm 0.20\text{mm}$, $0.56 \pm 0.17\text{mm}$ and $0.23 \pm 0.16\text{mm}$, respectively, for Cartesian-based sampling with SP=20% and $0.60 \pm 0.19\text{mm}$, $0.56 \pm 0.22\text{mm}$ and $0.42 \pm 0.15\text{mm}$, respectively, for radial-based sampling with SP=8% (32 spokes).

Conclusions—It is feasible to estimate VC-MRI from a single undersampled on-board 2D cine MRI. Phantom and patient studies showed that the temporal resolution of VC-MRI can potentially be improved by 5–10 times using a 2D cine image acquired with 10–20% k-space sampling.

I. INTRODUCTION

Minimizing target localization errors is crucial for effective radiation therapy. Previous studies showed that reduction of treatment errors was correlated with improved tumor control and reduced normal tissue toxicity. This is especially important for lung and liver cancer treatments due to the uncertainties caused by tumor motions (Keall *et al.*, 2006; Cervino *et al.*, 2009). Stereotactic body radiation therapy (SBRT) is an effective treatment paradigm in radiation therapy used to treat early stage non-small cell lung cancer and liver cancer. Compared to conventional radiation therapy, SBRT delivers much higher fractional dose with tighter PTV margins and longer treatment time, which makes SBRT more susceptible to treatment errors caused by both inter- and intra-fraction target motion. Therefore, on-board 4D or real-time volumetric verification of the target location before and during the SBRT treatment is critical (Zhang *et al.*, 2015; Zhang *et al.*, 2013; Ren *et al.*, 2014).

Cone-beam CT (CBCT) has been developed for on-board target localization; however, its applications are limited by the long scanning time, imaging dose and poor soft tissue contrast. Recently, radiotherapy units integrated with MRI have been developed for both inter- and intra-fraction verification. Compared to CBCT, MRI has better soft tissue contrast with no ionizing radiation dose to the patient. Different MRI techniques have been developed for localization of moving targets, including 2D cine MRI and 4D MRI (Cai *et al.*, 2011; Sarma *et al.*, 2014; Cervino *et al.*, 2011). 2D cine MRI tracks the 2D in-plane motion of the target by continuously generating 2D images of the patient. The limitation of 2D cine MRI is that it cannot capture the out of plane motion or the 3D deformation of the target due to the lack of volumetric information. Although orthogonal 2D MRI can be acquired to obtain the out of plane information, no clinically available techniques can be used to acquire them simultaneously or in a small enough time difference to achieve 3D verification or tracking (Mickevicius and Paulson, 2016; Breuer *et al.*, 2005). In addition, they still do not provide 3D information of the target, which is important for verifying/tracking the target deformation during treatment and post treatment evaluation of the accumulated dose delivered to the target.

4D MRI has been developed through either a prospective or a retrospective approach to provide full 4D spatial-temporal information of the target motion (Harris *et al.*, 2016; Deng *et al.*, 2016). However, prospective 4D MRI suffers from both poor temporal resolution (~1 s) and poor spatial resolution (4–5 mm) (Cai *et al.*, 2011). Retrospective 4D MRI usually suffers from long acquisition time (5–30 min) (Tryggstad *et al.*, 2013; Stemkens *et al.*, 2015; Han *et al.*, 2017; Cai *et al.*, 2011). Rank *et al.* 2017 developed a method to generate retrospective 4D MRI with an acquisition time of under 40 seconds, but the reconstruction time varied between 5.5 and 7.5 hours (Rank *et al.*, 2017). The long reconstruction time is due to the use of deformable image registration for motion compensation in each iteration, which is computationally extensive and time consuming. In addition, 4D MRI acquired with

2D MR sampling suffers from the same motion artifacts that have adversely affected 4D CT (Liu *et al.*, 2015).

To address the limitations of 2D cine and 4D MRI techniques, a volumetric cine MRI (VC-MRI) technique has been developed previously to use prior patient images, deformation models and real-time on-board 2D cine images to generate real-time 3D MRI images for both inter- and intra-fractional target localization (Harris *et al.*, 2016; Stemkens *et al.*, 2016; King *et al.*, 2012). The previous technique (Harris *et al.*, 2016) used a single, fully sampled 2D cine image to generate VC-MRI at a temporal resolution of 3–5 frames/s, which may not be sufficient to track a moving target for patients with short or irregular breathing cycles (Cervino *et al.*, 2011; Sarma *et al.*, 2014). Higher temporal resolution is also needed for VC-MRI to achieve better accuracy for post treatment accumulated dose evaluation and for deriving the tumor motion probability density function (PDF) for probability based treatments (Zhang *et al.*, 2012). Using accelerated 2D cine images also makes it feasible to acquire multiple 2D cine images at different locations for VC-MRI estimation to potentially improve its accuracy while maintaining a high temporal resolution. In this study, we investigate the feasibility of accelerating the temporal resolution of the VC-MRI by using undersampled 2D cine MRI to provide real-time 3D images of the patient. Two undersampling acquisition strategies were investigated, including Cartesian k-space undersampling and radial k-space undersampling. The effects of k-space sampling percentage and distribution, tumor sizes and noise on the VC-MRI estimation were investigated using both digital phantom and real patient data.

II. METHODS

II.A. VC-MRI ESTIMATION METHOD

4D MRI were acquired during the patient simulation stage. Patient respiratory motion modes were extracted from the deformation fields generated from the 4D-MRI data using principal component analysis (PCA). One phase of the prior 4D MRI was selected as the prior images designated as $\text{MRI}_{\text{prior}}$. The on-board VC-MRI images at each time step was considered as a deformation of $\text{MRI}_{\text{prior}}$. The deformation field for VC-MRI was represented as a linear combination of the prior motion modes, and the weightings for the motion modes were solved by matching to the on-board 2D cine MR images acquired in the data fidelity constraint. VC-MRI is then generated by deforming the $\text{MRI}_{\text{prior}}$ based on the deformation field solved.

A more detailed explanation of how the VC-MRI was estimated can be found in previous publications (Harris *et al.*, 2016).

II.B. ON-BOARD CINE MRI UNDERSAMPLING ACQUISITION

The on-board 2D cine MR images were retrospectively undersampled in k-space in order to substantially accelerate the VC-MRI to an ultrafast frame rate. Different undersampling acquisitions, including Cartesian-based sampling and radial-based sampling were studied to investigate the effect of sampling on the accuracy of the estimated VC-MRI. For each undersampling acquisition, sampling percentage (SP) was defined as the percentage of the

full k-space sampling. For an image size of 256×256 , full k-space sampling has 256 phase encoded lines sampled for Cartesian-based sampling and 402 ($256 \times \pi/2$) spokes sampled for radial-based sampling. The undersampled k-space data were used to reconstruct the 2D cine image using an iterative MR reconstruction algorithm with total generalized variation (TGV) regularization (Wang *et al.*, 2016). VC-MRI was then estimated using the 2D cine MRI reconstructed from the undersampled data. VC-MRI estimated from the fully sampled 2D cine MRI was also generated for comparison.

II.B.1. CARTESIAN-BASED VARIABLE DENSITY SAMPLING—Sampling profiles defined in a Cartesian coordinate system are straightforward and are suitable for easy implementation. In this study, variable density sampling along the phase-encoding direction was employed. For a Cartesian based undersampling with certain SP, k-space was sampled continuously from the center for a certain amount, and the rest of the k-space was sampled randomly. The central percentage (CP) was defined as the percentage of SP sampled continuously from the center. Various Cartesian-based undersampling strategies were employed to investigate the effect of SP and CP on the VC-MRI estimation scheme. In our study, SP of 20% and 10% were used, corresponding to an accelerated frame rate (FR) of 5x and 10x, respectively. For each SP, CP of 90%, 70% and 50% were investigated.

II.B.2 RADIAL-BASED SAMPLING—In radially sampled MRI, the k-space was sampled with equally spaced radial lines, all of which traversed the center of k-space. Undersampling in the azimuthal direction maintains the overall image structure and results in streaks instead of backfolding or discrete ghosting artifacts typically observed with Cartesian sampling. In this work, undersampled radial-based k-space data were generated by retrospectively undersampling full k-space data defined on a Cartesian grid along radial sampling lines (Smith *et al.*, 2012). Two radial sampling schemes were explored. The first sampling scheme used spokes spaced by the golden angle, i.e. constant azimuthal increment of 111.25° , with spoke numbers $N = 32$ and 21 used to sample the 2D cine MRI k-space data. The spoke numbers were chosen based on previous publications (Wang *et al.*, 2016). This golden angle of 111.25° is related to the Golden Ratio and causes radial lines to be evenly spaced with time (Winkelmann *et al.*, 2007). The second radial sampling scheme used was based on even-distributed sampling profiles, with azimuthal increments of 5.625° and 8.57° which result in spoke numbers $N = 32$ and 21 , respectively. The radial sampling with 32 and 21 spoke numbers represents a k-space SP of approximately 8% and 5.2%, respectively.

II.C. SIMULATION STUDY USING XCAT PHANTOM

A digital anthropomorphic phantom, 4D Extended Cardiac-Torso (XCAT) (Segars *et al.*, 2010), was used to simulate the prior 4D MRI set, the onboard ground-truth VC-MRIs and the 2D cine MRIs. Details regarding XCAT generation can be found in our previous publication (Harris *et al.*, 2016). To summarize, a 30 mm diameter spherical tumor was simulated in the middle of the lung in XCAT. The tumor intensities were Gaussian-distributed throughout the volume as to mimic a more realistic, heterogeneous tumor. A 10-phase 4D MRI was simulated as the prior 4D MRI, with a respiratory cycle of 5 seconds, and peak-to-peak amplitudes of the diaphragm curve and chest wall curves were set to 3 and 2 cm, respectively. The MRI volume of each phase was composed of $256 \times 256 \times 100$

voxels, with each voxel measuring $1.875 \times 1.875 \times 3.000 \text{ mm}^3$. The XCAT phantom was generated in the activity mode in order to produce MRI-like images. The end-expiration phase of the 4D MRI was selected as $\text{MRI}_{\text{prior}}$. On-board ground-truth VC-MRI were simulated the same as was done in our previous work (Harris *et al.*, 2016).

To evaluate the effects of potential patient breathing pattern change from simulation to treatment, 4 scenarios were simulated for the on-board volumetric cine-MRI sets, as follows: (1) no breathing pattern change; (2) for both body and tumor volume, the peak-to-peak amplitude of the diaphragm curve changes to 2 cm, and that of the chest wall curve changes to 1.2 cm; (3) body and tumor move according to different diaphragm and chest wall curves: the peak-to-peak amplitudes of the diaphragm curve for body volume and tumor are 4 and 2 cm, respectively, and those of the chest wall curve for body volume and tumor are 3 and 1.2 cm, respectively; and (4) based on scenario 2 but with the tumor having 20% phase shift relative to the body volume respiratory cycle.

Two-dimensional slices were extracted from the ground-truth VC-MRI at the location corresponding to the central slice of the tumor in the $\text{MRI}_{\text{prior}}$ image to simulate fully-sampled on-board 2D cine MRI acquired. The resolution of the 2D cine images was $1.875 \times 1.875 \text{ mm}^2$ and the slice thickness was 3.000 mm. These fully-sampled on-board 2D cine MR images were then transformed to k-space using direct Fourier transformation, and undersampled for the different undersampling acquisition strategies described above.

Based on results presented in our previous publication (Harris *et al.*, 2016), using fully sampled cine images showed that matching to a region-of-interest (ROI) around the tumor in the sagittal cine image resulted in the best VC-MRI accuracy across all XCAT scenarios. Because of this, VC-MRI generated in this study were based on matching to an ROI in the sagittal undersampled cine images.

II.C.1. NOISE STUDY—To investigate the effects of noise on the estimation accuracy of the accelerated VC-MRI, noise was incorporated into the 4D MRI and the undersampled 2D sagittal cine images for XCAT scenario 2, using a previously reported method (Harris *et al.*, 2016). The noise was added based on the assumption that the MRI signal is governed by a Rayleigh distribution in the presence of noise (Andersen, 1996). Signal-to-noise ratio (SNR) levels of 500, 100, 50 and 20 within the tumor based on the cine images in image space were tested.

II.C.2. TUMOR SIZE STUDY—To evaluate the effect that tumor size has on the estimation accuracy, a 4D MRI image set was generated with similar properties as described above, with the tumor diameter instead being 40 mm and 20 mm. The on-board VC-MRI images were generated based on a breathing pattern change of scenario 2 for the various tumor sizes. Cartesian-based undersampling with $\text{SP} = 20\%$, $\text{CP} = 90\%$ and $\text{SP} = 10\%$, $\text{CP} = 90\%$ were used for 2D cine image acquisition.

II.D. PATIENT STUDY

The accelerated VC-MRI technique was evaluated using 4 liver cancer patients, scanned on a GE Scanner under an institutional review board-approved protocol. Details of image

acquisition and 4D MRI reconstruction can be found in our previous publications (Cai *et al.*, 2011; Liu *et al.*, 2014; Harris *et al.*, 2016; Yang *et al.*, 2014). To briefly summarize, a Balanced Steady State Free Precession (bSSFP) imaging acquisition technique was used to acquire either 2D axial or sagittal images continuously and then retrospectively sort the images based on respiratory phases to generate 4D MRI. 2D cine MRI were acquired continuously for 2 minutes along each orientation after the 4D MRI scan. Both the prior 4D-MRI and on-board 2D cine MRI have a resolution of $\sim 1.9 \times 1.9 \text{ mm}^2$ with a slice thickness of 5mm. The temporal resolution was ~ 3 frames/s for the cine acquisition. For this study, both Cartesian and radial undersampling acquisition were investigated by retrospectively undersampling the 2D cine images acquired in the k-space. SP = 20% with CP = 90% was used for the Cartesian sampling, and N = 32 spokes spaced by the golden angle was used for the radial sampling. The undersampled 2D cine images were then reconstructed from the undersampled k-space data using the TGV iterative method. It is important to note that both the Cartesian and radial undersampled k-space data was retrospectively sampled from the original fully-sampled Cartesian-based k-space data.

II.E. EVALUATION METHODS

For the XCAT studies, the estimation accuracy for tumor location and volume in the on-board VC-MRI was evaluated at every cine time-step, and the results were reported as averages across the time-steps with corresponding standard deviations. Tumors were automatically contoured in 3D in an in-house MATLAB (MathWorks, Natick, MA) code based on a threshold voxel value in both the estimated images and the ground-truth VC-MRI images for comparison. Two metrics were defined to quantify the accuracy of the estimated tumor volume: volume percent difference (VPD) and center-of-mass shift (COMS) (Harris *et al.*, 2016)

For the patient studies, a previously developed ROI feature-based motion tracking method (Cai *et al.*, 2011) was used to calculate and compare the tumor tracking based on VC-MRI and the 2D cine images acquired along different directions. The 2D sagittal cine was used to track the tumor motion along the AP direction, and the 2D coronal cine was used to track the tumor motion along the SI and lateral directions. The tumor tracking curve determined from the sagittal and coronal 2D cine images was used as the reference to evaluate the accuracy of the tumor tracking curve extracted from the VC-MRI. Since the sagittal and coronal cine images were acquired sequentially instead of simultaneously, there may be some variations of tumor motion from sagittal to coronal cine acquisition. To resolve this issue, the average tumor tracking curves over the 2 minute acquisition for both 2D cine and VC-MRI were used to minimize the effects of breathing variations from cycle to cycle. Pearson correlation coefficients were also calculated between the tumor tracking curves extracted from the 2D cine images and the estimated VC-MRI.

III. RESULTS

VC-MRI generated using fully-sampled cine images were used as the reference for comparison with the VC-MRI generated using undersampled cine images, and will be referred to as ‘reference’ data from here on.

III.A. XCAT STUDY

III.A.1. CARTESIAN-BASED VARIABLE DENSITY SAMPLING—Table 1 shows the VC-MRI estimation accuracy for different scenarios using 2D cine MR sampled with SP = 20% and 10% and various CP in the k-space. The first column describes the amount of SP and CP that the VPD and COMS numbers correspond to. The second, third, fourth and fifth columns show the results for the XCAT scenarios 1, 2, 3 and 4, respectively. The top half of the table shows the VPD values and the bottom half of the table shows the corresponding COMS values. Figure 1a shows prior MRI image (end expiration phase of prior 4D MRI), ground-truth VC-MRI, estimated VC-MRI and their profile comparisons to provide qualitative comparisons of the estimated images. The cine MR used for VC-MRI estimation was sampled with SP = 10% and CP = 90%. Based on the profile curves and figures, the estimated VC-MRI matched well to the ground-truth VC-MRI. Figure 1b shows the subtraction images for the axial, coronal and sagittal images shown in Figure 1a, as well as the subtraction images between ground-truth VC-MRI and estimated VC-MRI using fully sampled cine image for comparison. From the subtraction images, the estimated VC-MRI using fully sampled cine images and the estimated VC-MRI using undersampled cine images both showed minimal difference from the ground-truth VC-MRI in the target region.

III.A.2 RADIAL-BASED SAMPLING—Data in Table 2 shows VPD and COMS values for estimation based on various amounts of radial sampling in the sagittal cine images across all XCAT scenarios. Using the golden angle distribution resulted in slightly better accuracy than using even distribution.

III.A.3 EFFECTS OF NOISE—Table 3 shows VPD and COMS values for XCAT scenario 2 with various amounts of noise added to the undersampled sagittal cine images. The Cartesian-based sampled images were generated by sampling 10% of total k-space (SP = 10%) with 90% of that sampled in the center k-space (CP=90%). The radial-based sampled images were generated by sampling with the golden angle using 21 spokes. VC-MRI was robust against increasing noise levels for both Cartesian-based and radial-based undersampling.

III.A.4 EFFECTS OF TUMOR SIZE CHANGE—Data in Table 4 shows VPD and COMS values for XCAT Scenario 2 using a 20 mm, 30 mm and 40 mm diameter tumor. Cartesian-based undersampling was used in this study. Results shown are for the end-inspiration time-step. The term ‘reference’ refers to VC-MRI estimation based on using a fully sampled sagittal cine image. With a decreased tumor size of 20 mm, the VC-MRI accuracy decreased when undersampling percentage decreased. With an increased tumor size of 40 mm, the VC-MRI was accurate with both SP = 20% and SP = 10%.

III.B. PATIENT STUDY

In the patient studies, the 2D cine images acquired were considered as the corresponding slices of the ground-truth VC-MRI to evaluate the accuracy of the estimated VC-MRI based on undersampled cine images. Figure 2a shows prior MRI image at end-inspiration phase, 2D cine at an end-expiration phase, estimated VC-MRI at an end-expiration phase and their normalized profile comparisons for patient 1. Figure 2b shows subtraction images between

estimated accelerated VC-MRI and 2D cine for patient 1, as well as the subtraction images for 2D cine and estimated VC-MRI based on fully sampled cine images. Note that the accelerated VC-MRI was estimated based on SP = 20%, CP = 90% on Cartesian grid in the axial, sagittal and coronal cine images. The red arrows indicate the areas for comparison. Figure 2c shows the tumor tracking based on the fully sampled 2D cine images at different views, the estimated VC-MRI based on the fully sampled 2D cine images and the estimated VC-MRI based on the undersampled 2D cine images for average cycles in the lateral, SI and AP directions (Harris *et al.*, 2016). The accelerated VC-MRI and non-accelerated VC-MRI were estimated based on sagittal cine images. The tracking along the SI and lateral directions were based on the coronal slice of the accelerated VC-MRI and non-accelerated VC-MRI and coronal 2D cine images, and the tracking along the AP direction was based on sagittal slices. Table 5 shows the mean and standard deviation, as well as the Pearson correlation coefficient, of the target tracking accuracy based on VC-MRI using fully sampled 2D sagittal cine images and accelerated VC-MRI using undersampled 2D sagittal cine images for various undersampling acquisition strategies in each patient. All Pearson correlation coefficients were greater than 0.900.

DISCUSSION

Patient data showed that we can achieve high quality and high temporal resolution VC-MRI using ultra-fast cine images acquired with 10–20% SP for various undersampled acquisition strategies, which corresponds to a 5–10 times acceleration rate of the temporal resolution. This improvement of temporal resolution can potentially improve the localization/tracking accuracy based on VC-MRI to minimize the treatment errors of SBRT to improve the tumor control and minimize the normal tissue toxicities.

In our studies, VPD and COMS were used as metrics for evaluating the accuracy of VC-MRI. Note that the accuracy that can be achieved by VC-MRI is limited by the image resolution of the prior 4D MRI and on-board 2D cine MRI acquired. In our studies, both the prior 4D-MRI and on-board 2D cine MRI have a resolution of $1.875 \times 1.875 \times 3.000 \text{ mm}^3$ for XCAT data and $1.9 \times 1.9 \times 5.0 \text{ mm}^3$ for patient data. Therefore, we consider COMS within 2 mm as acceptable for VC-MRI estimation. VPD is sensitive to the target size and tends to be larger for smaller targets and smaller for larger targets, as it is calculated by dividing the target volume differences by the actual target volume size. Assuming the target volume is offset by 2 mm (the tolerance for COMS), the VPD for a 2 cm, 3 cm and 4 cm diameter target will be 28.9%, 19.4%, 14.2%, respectively, which were used as the tolerance for VPD in our studies.

IV.A. EFFECTS OF UNDERSAMPLING ACQUISITION STRATEGIES

In the XCAT study, Cartesian sampling and radial sampling achieved accurate VC-MRI estimation when 10% and 5.2% of total k-space were sampled, respectively. For Cartesian based undersampling, sampling more signal in the central k-space, i.e. higher CP, led to better accuracy in the VC-MRI estimation. This can be explained by the fact that the central k-space region maintains the information about the gross anatomical structures of the patient, which are important for solving the PCA coefficients in the VC-MRI estimation.

Additionally, it is important to note that sampling with a low SP but high CP is essentially similar to acquiring a lower resolution image. For the radial based undersampling, using golden angle distribution achieved slightly better accuracy than using even distribution.

In the patient study, using Cartesian-based undersampling produced accurate VC-MRI estimation when sampling 20% on Cartesian grid. Using radial-based sampling, VC-MRI estimation was accurate when using the golden angle with 32 spokes (SP=8%).

IV.B. EFFECTS OF TUMOR SIZE

In the XCAT study, VC-MRI estimation for a larger diameter tumor (40 mm diameter) resulted in accurate estimation when using the sagittal cine image acquired with 10% sampled k-space data, as shown in Table 4. When the XCAT tumor shrunk to 20 mm diameter, the VC-MRI estimation accuracy was reduced while still using 10% of total k-space for 2D cine image acquisition. Increasing with the sampling percentage to 20% of k-space improved the VC-MRI estimation accuracy for smaller tumors. This suggests that more k-space sampling is needed for smaller tumors in the VC-MRI estimation, mainly because there is less anatomical information in smaller tumors that can be used to determine the PCA coefficients. Also note that smaller tumors tend to lead to larger VPD values due to the sensitivity of VPD to the actual target volume. Another solution for VC-MRI estimation with small tumors is to use higher spatial resolution 4D MRI and cine images. This is because more anatomical information is provided in the fine resolution images to solve for the PCA coefficients. In addition, it also improves the resolution of contouring the tumor volume, which is important for the accuracy of the VPD and COMS calculation for small tumors.

IV.C. CLINICAL RELEVANCE AND LIMITATIONS

Using accelerated 2D cine images allows us to substantially improve the temporal resolution of the VC-MRI compared to using fully-sampled 2D cine images. This may improve moving target verification/tracking for patients with short or irregular breathing cycles. In addition, higher temporal resolution allows us to achieve better accuracy for post treatment accumulated dose evaluation and for deriving the tumor motion probability density function for probability-based treatments. (Zhang *et al.*, 2012)

Using accelerated 2D cine images also makes it feasible to acquire multiple 2D cine images for VC-MRI estimation to potentially improve the accuracy while maintaining a high temporal resolution. To give an example of this, an XCAT simulation was performed to investigate the effect of number of sagittal cine images on the accuracy of VC-MRI. Based on XCAT on-board scenario 2, when the number of 2D sagittal cine images increased from 1 to 10, the VPD/COMS for EOI phase improved from 9.33%/0.54mm to 4.76%/0.10mm based on Cartesian undersampling.

It is important to note that this study aimed to investigate the feasibility of using accelerated 2D cine images for VC-MRI estimation. Undersampling the k-space data is just one approach we explored for accelerating the 2D cine acquisition. There are other alternative methods, such as parallel imaging and reducing cine image resolution, which can also be

used to accelerate 2D cine imaging for VC-MRI estimation. The efficacy of these alternative techniques for accelerating VC-MRI estimation will be investigated in future studies.

As stated above, in the current study, VC-MRI is estimated based on the 2D cine images reconstructed from the under sampled data. An alternative approach is to estimate VC-MRI directly from the undersampled k-space data, which can be computationally more efficient by skipping the 2D cine reconstruction process. However, it is challenging to implement this method based on the current VC-MRI estimation scheme. Due to the limitations of the motion model extracted by the PCA, VC-MRI estimation requires matching to an ROI around the target region in the image domain to account for day-to-day patient breathing variations, as demonstrated in our previous study (Harris *et al.*, 2016). This requirement cannot be satisfied when estimating VC-MRI directly from the k-space, since the signal from the ROI region in the image domain cannot be separated from signals in other regions in the k-space. The problem can potentially be resolved by developing an advanced motion modeling technique that models the relative organ motions in local regions to account for breathing variations. This method is still under development and further work is warranted.

The VC-MRI estimation has been evaluated by using both the 4D digital XCAT phantom and patient data in a retrospective approach in this study. The usage of XCAT provided several unique benefits: 1). Ground truth images are available for the evaluation of VC-MRI. 2). XCAT has the flexibility to simulate different patient breathing patterns, tumor sizes and noise levels to study their individual effects on the VC-MRI estimation so that VC-MRI can be better implemented for patient studies. The limitations of XCAT phantom are that they are simulated images with simplified anatomies. Future studies may incorporate more MR artifacts, such as ringing or blurring artifacts to make the images closer to clinical data. Additionally, undersampling artifacts were not simulated in the XCAT study, and future implementation of such artifacts would be beneficial.

In the retrospective patient study, the VC-MRI was evaluated using four liver cancer patients' data. It is challenging to establish ground-truth images for patient studies since currently there is no real time 3D MRI imaging technique available. In our study, tumor tracking curves extracted from orthogonal fully sampled 2D cine images were used as the references to evaluate the tumor tracking curves determined by the accelerated VC-MRI. Future studies may look into ways to better assess estimation accuracy in the retrospective study. For example, acquiring another 4D-MRI taken at a different time than prior 4D-MRI, and using the second 4D-MRI as the ground-truth to fully evaluate the accuracy of the VC-MRI in terms of tracking the tumor trajectory and reconstructing the 3D tumor volume. It is also worthy to mention that only retrospective patient data are included in the current study to evaluate the feasibility of accelerating the VC-MRI technique. Compared to prospective studies, retrospective studies have the advantages of providing the ground-truth images for evaluation and having the flexibility to investigate the effects of various under sampling strategies as well as various amounts of under sampling (Sarma *et al.*, 2014; Subashi *et al.*, 2013; Wang *et al.*, 2016). However, retrospective studies do not account for certain challenges in prospective in-vivo applications of the technique, such as undersampling artifacts, timing errors, gradient imperfections and Eddy currents in the MR acquisition. Therefore, future prospective patient studies are warranted to fully evaluate the VC-MRI

technique for clinical applications. Challenges with establishing ground-truth images in the prospective studies need to be resolved before VC-MRI can be evaluated in the prospective study. Additionally, it is important to note that both the Cartesian and radial undersampled k-space data was retrospectively generated by sampling the original fully-sampled Cartesian-based k-space data in the patient study. No radial k-space data were actually acquired. Radial k-space data generated from Cartesian k-space data may not be equivalent to the actual acquired radial k-space data, due to effects of gradient non-ideality, main field inhomogeneity and magnetic susceptibility. Because of this, radial k-space data will be acquired in the future prospective studies to further evaluate the accuracy of VC-MRI using radial undersampling.

Lastly, current processing time for VC-MRI estimation is ~2 minutes using in-house MATLAB programs, with ~1 minute to reconstruct the undersampled 2D cine images and ~1 minute to estimate the VC-MRI. Additional work is needed to accelerate the program using the graphics card, parallel computing or algorithm/code optimization to reduce the processing time to seconds to achieve real time 3D imaging with minimal latency time. Another point to make is that the VC-MRI estimation at different time steps are completely independent, and therefore they can be computed in parallel. During the implementation, although the calculation time causes a delay initially for generating VC-MRI at the first time step, VC-MRI at the following time steps will be generated continuously at the same temporal resolution as the accelerated 2D cine acquisition. Intrinsically, the generation of VC-MRI at all time steps has a latency period equal to the processing time. Acceleration strategies are being developed to reduce this intrinsic latency period from ~2 mins to seconds.

IV. CONCLUSION

Our study showed that it is feasible to estimate VC-MRI from patient prior data, motion modeling and undersampled on-board 2D cine images. Using the undersampled 2D cine images, the temporal resolution of VC-MRI can be improved by 5–10 times for various k-space sampling strategies to provide real time 3D target localization or tracking in lung and liver SBRT treatments.

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Figure 1.

a) Comparison of prior MRI (MRI_{prior}) at end-expiration phase, ground-truth on-board volumetric cine-MRI ($VCMRI_{GT}$) at end-inspiration phase and estimated on-board VCMRI ($VCMRI_{Acc.Est}$) for XCAT Scenario 2. ‘Acc’ refers to VC-MRI based on accelerated 2D cine images. The undersampled sagittal cine image was acquired using $SP = 10\%$ and $CP = 90\%$. The horizontal red dotted line corresponds to the location of the profile curves shown to the right of the images. **b)** Subtraction images for axial, coronal and sagittal images shown in a). The subtraction images between ground-truth VC-MRI and estimated VC-MRI based on fully sampled cine images are also shown for comparison.

Figure 2.

a) Prior MRI image at end-inspiration phase, 2D cine at an end-expiration phase, estimated VC-MRI for patient 1. VC-MRI was estimated by matching to undersampled axial, coronal and sagittal cine images, respectively. The undersampled cine images were generated by using $SP = 20\%$ and $CP = 95\%$. Horizontal red dotted lines correspond to the location of the normalized profile curves, shown to the right of the images. The red arrows indicate the areas for comparison. b) Subtraction images for axial, coronal and sagittal images shown in a). The subtraction images between 2D cine and estimated VC-MRI based on fully sampled cine images are also shown for comparison. The red arrows indicate the areas for

comparison. c) Tumor tracking curves based on 2D cine, VC-MRI using full sampled sagittal cine images ($VC-MRI_{est}$), and VC-MRI using Cartesian-based undersampled sagittal cine images ($VC-MRI_{acc,est}$) for an average cycle ($SP=20\%$, $CP=90\%$). The tracking along the lateral and superior-inferior directions was based on the coronal slice of the accelerated VC-MRI and non-accelerated VC-MRI and coronal cine, whereas tracking along the anterior-posterior direction was based on the sagittal slice of accelerated VC-MRI and non-accelerated VC-MRI and sagittal cine.

Table 1

Comparison for SP = 20% and SP = 10% with various amounts of CP. VPD and COMS results were averaged across all cine time-steps. The reference row corresponds to VC-MRI generated with cine images using SP = 100%.

Scenarios	1	2	3	4
VPD(%)				
Reference (SP=100%)	9.52±1.74	8.96±1.43	8.98±1.51	8.93±1.47
CP (SP=20%)				
90%	10.78±2.83	9.01±2.04	11.54±3.37	11.54±3.37
70%	10.10±1.84	9.31±1.77	10.95±4.17	11.81±4.57
50%	10.52±2.10	9.79±2.24	11.60±3.58	12.41±4.56
CP (SP=10%)				
90%	10.89±2.87	10.17±3.70	12.73±5.73	13.91±5.94
70%	13.51±5.25	11.96±4.85	14.45±6.64	14.25±6.36
50%	18.48±8.52	16.01±6.72	20.63±9.11	18.61±8.73
COMS(mm)				
Reference (SP=100%)	0.53±0.20	0.43±0.20	0.43±0.21	0.43±0.20
CP (SP=20%)				
90%	0.73±0.25	0.61±0.31	0.79±0.47	0.79±0.47
70%	0.63±0.23	0.53±0.24	0.75±0.55	0.92±0.61
50%	0.71±0.30	0.61±0.32	0.86±0.53	0.98±0.62
CP (SP=10%)				
90%	0.80±0.31	0.72±0.36	1.00±0.61	1.07±0.78
70%	1.12±0.71	1.03±0.63	1.33±0.83	1.29±0.80
50%	1.78±1.05	1.53±0.82	2.08±1.11	1.81±1.06

Comparison among various amounts of radial sampling using the golden angle and even distribution VPD and COMS results were averaged across all cine time-steps. The reference row corresponds to VC-MRI generated with cine images using SP = 100%.

Table 2

Scenarios		1	2	3	4
		VPD(%)			
Reference	SP=100%	9.52±1.74	9.52±1.74	9.52±1.74	9.52±1.74
Spoke Number	SP (%)				
32	8	Golden Angle 9.92±1.72	9.54±1.45	10.69±3.13	11.68±3.98
		Even Distribution 10.16±1.81	9.71±1.94	11.32±3.46	11.87±4.25
21	5.2	Golden Angle 10.75±2.03	10.26±1.82	12.17±3.81	12.93±3.52
		Even Distribution 11.24±1.71	12.47±3.78	15.25±3.59	14.82±5.57
		COMS(mm)			
Reference	SP=100%	0.53±0.20	0.43±0.20	0.43±0.21	0.43±0.20
Spoke Number	SP(%)				
32	8	Golden Angle 0.59±0.21	0.55±0.23	0.75±0.43	0.88±0.53
		Even Distribution 0.65±0.24	0.58±0.30	0.83±.48	0.88±0.60
21	5.2	Golden Angle 0.80±0.26	0.67±0.33	0.85±0.49	1.09±0.47
		Even Distribution 0.82±0.29	1.11±0.75	1.44±0.48	1.39±0.91

VPD and COMS for XCAT scenario 2 with various amounts of noise added to the undersampled cine images. VPD and COMS results were averaged across all cine time-steps. The reference row corresponds to VC-MRI generated with cine images using $SP = 100\%$.

Table 3

SNR	500	100	50	20
VPD(%)				
Reference	SP=100%	9.52±1.74	9.52±1.74	9.52±1.74
SP(%)				
Cartesian	10	10.28±2.44	9.84±2.75	10.54±2.87
Radial, GA	5.2	11.00±2.68	10.10±2.19	10.54±2.92
COMS(mm)				
Reference	SP=100%	0.53±0.20	0.43±0.20	0.43±0.21
SP(%)				
Cartesian	10	0.65±0.30	0.63±0.40	0.75±0.38
Radial	5.2	0.71±0.39	0.62±0.25	0.67±0.31

Table 4

VPD and COMS values for XCAT Scenario 2 using a 20 mm, 30 mm and 40 mm diameter tumor. Cartesian-based undersampling was used. Both the 20% and 10% k-space images were sampled with CP = 90%. Results shown correspond to the end-inspiration phase of the VC-MRI. Here, ‘reference’ refers to VC-MRI estimation based on using a fully sampled sagittal cine image (SP=100%).

	Reference (SP=100%)	SP = 20%	SP = 10%
Tumor Diameter		VPD(%)	
20 mm	10.77	11.43	24.22
30 mm	8.00	7.88	9.33
40 mm	6.74	7.41	7.27
		COMS(mm)	
20 mm	0.68	0.52	1.66
30 mm	0.29	0.16	0.54
40 mm	0.72	0.62	0.65

Table 5

Tumor tracking errors ($\mu \pm \sigma$ (mm)) and Pearson correlation coefficients (PCC) based on comparing estimated VC-MRI with 2D sagittal and 2D coronal cine images in SI, AP and lateral directions for the patient study. Reference VC-MRI is based on using fully sampled cine images (SP=100%). Cartesian-based undersampling VC-MRI_{acc} were generated with SP = 20% and CP = 90%. Radial-based undersampled VC-MRI_{acc} were generated with using the golden angle and N = 32 spokes (SP=8%).

Patient		SI		AP		LAT	
		$\mu \pm \sigma$ (mm)	PCC	$\mu \pm \sigma$ (mm)	PCC	$\mu \pm \sigma$ (mm)	PCC
1	Reference VC-MRI	0.52±0.46	0.982	0.21±0.09	0.998	0.28±0.14	0.999
	Cartesian-based VC-MRI _{acc}	0.40±0.37	0.987	0.30±0.28	0.978	0.07±0.05	0.997
	Radial-based VC-MRI _{acc}	0.46±0.27	0.995	0.21±0.20	0.989	0.14±0.07	0.993
2	Reference VC-MRI	0.32±0.17	0.985	0.04±0.02	0.999	0.56±0.54	0.929
	Cartesian-based VC-MRI _{acc}	0.56±0.36	0.956	0.38±0.20	0.968	0.57±0.56	0.927
	Radial-based VC-MRI _{acc}	0.51±0.43	0.939	0.11±0.03	0.997	0.61±0.33	0.941
3	Reference VC-MRI	1.04±0.39	0.992	1.08±0.58	0.905	0.71±0.33	0.920
	Cartesian-based VC-MRI _{acc}	0.41±0.35	0.994	0.96±0.51	0.907	0.02±0.01	0.999
	Radial-based VC-MRI _{acc}	1.04±0.48	0.992	1.16±0.62	0.900	0.43±0.37	0.959
4	Reference VC-MRI	0.26±0.20	0.995	0.65±0.42	0.921	0.30±0.30	0.924
	Cartesian-based VC-MRI _{acc}	0.46±0.47	0.978	0.61±0.32	0.934	0.27±0.29	0.938
	Radial-based VC-MRI _{acc}	0.37±0.28	0.991	0.77±0.58	0.918	0.50±0.33	0.924