A feasibility study on 3D image reconstruction from 2D orthogonal cine-MRI for MRI-guided radiotherapy

Running Title: 3D reconstruction from 2D cine-MRI

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Conflict of interest
Paul Keall is a stakeholder in SeeTreat, a start-up company to commercialize intellectual property generated through NHMRC program grant APP1036075.. Other authors have no conflict of interest.

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Abstract

Purpose: In-room MRI is a promising image guidance strategy in external beam radiotherapy to acquire volumetric information for moving targets. However, limitations in spatio-temporal resolution led several authors to use 2D orthogonal images for guidance. The aim of this work is to present a method to concurrently compensate for non-rigid tumor motion and provide an approach for 3D reconstruction from 2D orthogonal cine-MRI slices for MRI-guided treatments.

Methods: Free-breathing sagittal/coronal interleaved 2D cine-MRI were acquired in addition to a pre-treatment 3D volume in two patients. We performed deformable image registration (DIR) between cine-MRI slices and corresponding slices in the pre-treatment 3D volume. Based on an extrapolation of the interleaved 2D motion fields, the 3D motion field was estimated and used to warp the pre-treatment volume. Due to the lack of a ground truth for patients, the method was validated on a digital 4D lung phantom.

Results: On the phantom, the 3D reconstruction method was able to compensate for tumor motion and compared favorably to the results of previously adopted strategies. The difference in the 3D motion fields between the phantom and the extrapolated motion was 0.4±0.3mm for tumor and 0.8±1.5mm for whole anatomy, demonstrating feasibility of performing a 3D volumetric reconstruction directly from 2D orthogonal cine-MRI slices. Application of the method to patient data confirmed the feasibility of utilizing this method in real world scenarios.

Conclusions: Preliminary results on phantom and patient cases confirm the feasibility of the proposed approach in an MRI-guided scenario, especially for non-rigid tumor motion compensation.

1. Introduction

Variability of organ shape and position in thoracic and abdominal regions due to breathing is an important issue in radiotherapy treatment [1] and needs to be compensated for to increase accuracy in target localization and dose delivery [2]. For this purpose, in-room image guidance is increasingly utilized for motion management [3]. Due to its exquisite soft tissue contrast, the ability to select arbitrary imaging planes, and the absence of imaging dose, Magnetic Resonance Imaging (MRI) is an ideal imaging modality to study organ motion [4,5], motivating several groups to develop integrated MRI-radiotherapy systems [6,7,8].

In current MRI scanners, real-time 3D image acquisitions during respiration is not feasible at clinically acceptable spatio-temporal resolution [9]. Fast dynamic MRI (i.e. cine-MRI) allows high temporal resolution imaging, but is limited to the acquisition of few 2D slices. The use of 2D cine-MRI for organ motion quantification has been widely reported in the literature [10,11,12,13], and is current standard of care for real-time imaging in the new in-room MRI systems. However, the need to accurately adapt for 3D motion is of primary importance to enable accurate treatments [14]. For this reason, the ideal imaging strategy for in-room MRI treatment systems would yield real-time 3D information of both tumor and surrounding tissues.

Several methods have been proposed in the literature to track tumor motion and derive its 3D local information based on 2D interleaved orthogonal cine-MRI slices [15,16,17,18]. These strategies rely on acquiring a pre-treatment 3D scan, extracting a target template and performing template matching between the template and pairs of orthogonal 2D cine-MRI intersecting the target motion path. However, such approaches provide only the rigid translational component of tumor motion.

Another solution able to derive the non-rigid global 3D anatomical information is to use a patient specific global motion model [19,20], which could be also used for dose accumulation [29]. In this approach, a motion model is constructed based on 4D planning data, and updated during treatment based on surrogate signals (e.g. surface information or fiducial markers). Two recent works by Harris et al. [21] and Stemkens et al. [22] extend the use of global motion models to the MRI-guided scenario. Limitations of both approaches lay on (i) the use of a single surrogate to update the model based on a weighting factor derived from the calculation of a similarity metric between model and 2D cine-MRI (sagittal or coronal) and (ii) the sensitivity of the training dataset to inter- and intra-fraction changes. As suggested by [21], the impact of patient breathing variability between pre-treatment and on-board imaging needs to be studied further in the implementation of global motion models, since the correct estimation of tumor motion is the primary step for accurate tumor tracking treatments.

The aim of this work is to provide an alternative strategy to solve limitations of template matching and global motion models in tumor motion compensation for MRI-guidance. We propose a novel 3D reconstruction method directly from the 2D orthogonal sagittal/coronal cine-MRI slices acquired during treatment by means of deformable image registration (DIR) between the cine-MRI slices and a pre-treatment 3D volume. Figure 1 shows a comparison of the proposed method with respect to the literature in a clinical MRI-guided workflow. Our method is able to directly capture the local 3D non-rigid motion of the tumor, hence increasing tumor motion compensation accuracy. The proposed method additionally was also evaluated as a potential approach to provide a preliminary estimate of the global anatomy.

2. Materials and Methods

2.1. Dataset

a. Phantom Dataset

A phantom dataset was used for validation, since able to produce a consistent ground truth. Two different cases were generated using the XCAT lung phantom [23]. Exhale/inhale phases were generated and used respectively as *pre-treatment 3D* and *ground_truth*.
The first case considered a large breathing motion (i.e. 3cm motion in the SI direction at the diaphragm) with a tumor centered in the middle of the right lung lobe and image spacing of $1.5mm^3$.
The second case included a diaphragm motion of 16mm/4mm and a tumor motion of 8mm/4mm in SI/AP directions (where SI refers to superior-inferior, AP to anterior-posterior and RL to right-left). The tumor was located in the right lung with image spacing of $1mm^3$. For this latter case, an additional intermediate respiratory phase was obtained for comparison with a global motion model (see Section 2.3.b for details).

b. Patient Dataset

The patient dataset was composed of:
(i) Gated 3D volumes of coronal slices, acquired at the exhale and inhale respiratory phases to simulate pre-treatment acquisition (i.e. *pre-treatment3D*) and the in-room volume (i.e. *measured3D*), respectively. A spin echo T2-weighted sequence (SPACE) was used with spacing of $1.18\times1.18\times5mm^3$.
(ii) Free-breathing, 2D interleaved orthogonal sagittal/coronal cine-MRI images of the lung in two patients to simulate in-room acquisitions (i.e. *cineMRI*). A balanced steady-state free precession gradient echo T2/T1-weighted sequence (TrueFISP) was used (spacing of $1.48\times1.48\times5mm^3$; acquisition time: 300ms/slice) [24]. The acquisition of sagittal/coronal slices was centered in the tumor. The sagittal slice incorporates both the SI and the AP components, which are the main directions of respiratory motion. The coronal slice provides the remaining RL component, with redundant information regarding the SI motion.

2.2. 3D Reconstruction Method

The method to estimate a 3D volume from interleaved cine-MRI slices is based on the following steps (Figure 2):

(i) 2D DIR. 2D DIR was performed between the sagittal/coronal slices of the *pre-treatment3D* on the corresponding sagittal/coronal slices from the 2D cine-MRI (sagittal and coronal *cineMRI*) (Figure 2, Panel i).

(ii) 3D motion field extrapolation. The 2D sagittal and coronal motion fields components (vf_{sag_AP}, vf_{sag_SI}, vf_{cor_RL}, vf_{cor_SI}) obtained through DIR, were replicated to all the slices in the 3D space (e.g. the AP motion component as detected on the sagittal slice was replicated to all the other sagittal slices), assuming a correlation between cine-MRI motion and the whole anatomy. Redundant quantitative information was available in the SI direction (i.e. vf_{cor_SI} and vf_{sag_SI}), as the orthogonal cine-MRI images provide a measurement of the SI component on both the sagittal and coronal plane. Therefore, the overall SI component of the estimated motion field was modulated by computing the mean of the motion field SI components (Figure 2, Panel ii).

(iii) Estimated 3D image (Figure 2, Panel iii). Application of the estimated 3D motion field to the *pre-treatment3D* volume in order to obtain the *estimated3D* volume.

(iv) Analysis. Comparison between the *pre-treatment3D* volume and the *ground_truth* at the same respiratory phase (*measured3D* for patients).

To assist with understanding this paper, the four different image types used in this work and their role are described in Table 1.

2.3. 4D CT lung XCAT phantom

a. Evaluation of the 3D reconstruction method

The proposed approach was validated on the 4D XCAT phantom by extracting exhale/inhale sagittal and coronal slices to simulate the cine acquisition (c.f. *cineMRI* images in Figure 2). By setting the XCAT exhale image as a reference (*pre-treatment3D*), we applied the method in Section 2.2 to generate the volume at the inhale phase (*estimated3D*). The XCAT inhale image was used as ground truth (*ground_truth*).

For the phantom with 16mm/4mm motion in SI/AP, orthogonal cine-MRI slices were extracted with both a centered and a shifted location (5mm from the center) in the tumor. The shifted data were generated in order to simulate out-of-plane motion. No shifted slices were simulated on the 3cm motion case, due to the presence of respiratory motion only in the SI direction.

To analyze tumor tracking accuracy, we segmented the tumor and evaluated the distance of its Center Of Mass (COM) and the Dice coefficient between the *estimated3D* volume and the *ground_truth*.

The accuracy of the 3D reconstruction method in the surrounding anatomy was quantified by measuring the 3D diaphragm position [25]. For the phantom, a quantification on automatic anatomical landmarks [26,27] was also performed (for details see supplementary materials). An analysis on the motion fields was performed by comparing the estimated motion field (i.e. derived from 2D demons DIR, Section 2.2 point (i)) with the *pre-treatment3D/ground_truth* motion field obtained by means of a 3D b-spline DIR (www.plastimatch.org)[28].

b. Comparison with other methods

A comparison of the proposed 3D reconstruction method with template matching and global motion model approaches from the literature (as shown in Figure 1) was performed for the 16mm/4mm motion case:

- Template matching [16]: a template was created around the tumor of the *pre-treatment3D* and searched among *cineMRI*. The derived rigid transformation was applied to the *pre-treatment3D* to derive *estimated3D*, which was then compared with the *ground_truth*.
- Global motion model [20]: a model was built on the exhale volume and an intermediate respiratory phase (i.e. multiple *pre-treatment3D* volumes) by means of DIR and principal component analysis. The model was then updated according to the tumor motion extracted from *cineMRI*, to derive the *estimated3D* volume.

The performance of each method was quantified using the same approach described in Section 2.3.a.

2.4. Application to patient data

For patients, we applied the 3D reconstruction method as shown in Figure 2 and we compared the *estimated3D* and *measured3D* volumes in terms of tumor motion and diaphragm position. In addition, the same quantification was performed on the 2D corresponding slices of *cineMRI* vs. *estimated3D* and *cineMRI* vs. *measured3D,* to analyze the capability of the estimated volume to include the motion described by the cine-MRI and to provide a quantification of the variability of the inhale phase. As for the phantom, an analysis on the motion fields was performed. No landmark distance was computed on patients since *pre-treatment3D* and *cineMRI* used to derived *estimated3D* were acquired with different MR sequences and contrast, limiting automatic landmarks identification [26,27]. Comparison with other methods was not implemented in patients, since multiple (4D) pre-treatment volumes were not available for the creation of a motion model.

3. Results

3.1. 4D CT lung XCAT phantom

a. Performance of the 3D reconstruction method

The 3D reconstruction method showed a good agreement between the *estimated3D* volume and the *ground_truth* (Figure 3, Panel A), with distances close to *ground_truth*. For the 16mm motion case, 1mm distance in SI for tumor, 1.3±2.3mm for diaphragm and 1.6±3.2mm for landmarks were quantified (Table 2 and Figure E1 in supplementary materials). Slightly worse results were instead observed in the case of shifted cine-MRI slices (Figure 3, Panel B), with an error of 1-2mm in AP and SI for the COM.

Figure 4 shows an example of the *estimated3D* close and far with respect to cine-MRI location (distance from the tumor of [80,80,20]mm in axial, sagittal and coronal directions respectively), with corresponding motion fields. The difference (mean±std(95th percentile)) between the 3D estimated motion field and the ground truth motion field (i.e. 3D DIR between *pre-treatment3D/ground_truth*) was 0.8±1.5(3.4) mm and 0.8±2.1(3.7) mm for the 16mm lung tumor case with centered and shifted slices, respectively. A difference between the two motion fields of 0.4±0.3(0.5) mm was observed at the tumor location for the 16mm case. The variability far from cine-MRI intersection instead was higher and variations were visible in organs which were not included in the field of view of the cine-MRI slices, as visible in Figure 4 (panel B and C) near the heart. Specifically for the 3cm motion case, the difference in terms of motion field in the 3D reconstruction method was 1.6±3.8(4.2) mm. The estimated motion field was not significantly different from the ground truth motion field (Wilcoxon test, α=5%).

b. Comparison with other methods

Figure 5 shows the comparison of the proposed 3D reconstruction method with respect to other strategies. Image differences are reported between *estimated3D* and *ground_truth*. Quantitative analysis is shown in Table 3. For tumor region, lower errors were achieved by 3D reconstruction followed by template matching and global motion model. For surrounding anatomy, a good performance was achieved by global motion model approach and 3D reconstruction approach.

Higher differences were notable in the motion field with respect to the ground truth motion at the tumor location (0.9±0.7(1.1) mm for the global motion model while 0.4±0.3(0.5) mm for the 3D reconstruction). However, the overall motion field difference for global motion model was 0.4±1.7(0.9) mm (0.8±1.5(3.4) mm for 3D reconstruction), with slightly higher landmark distance for 3D reconstruction (1.6±3.2mm for 3D reconstruction against 1.2±1.4mm for motion model).

3.2. Patient data

The *estimated3D* volume shows a partial overlap with the *measured3D* (Figure 6), with lower performance in P01 near the tumor and with a diaphragm distance of about 4mm for both patients from the *measured3D* (Table 4).

However, a better overlap of *cineMRI* with *estimated3D* than with *measured3D* is shown in the tumor region and in the diaphragm for P01 and P02, respectively (Figure 7). By considering the coronal *cineMRI* and the corresponding slice in the *estimated3D* volume, the Dice coefficient and the COM distance were better in contrast to *cineMRI*/*measured3D.* This anticipate the limited accuracy of *measured3D* to be a use as ground truth for patient data, as discussed in Section 4.2. As such, in Table 4 we highlighted in grey the accuracy of *estimated3D* in describing the real in-room motion provided by the cine-MRI data, which is not instead provided by *measured3D* (i.e. pre-treatment volume used to simulate intra-treatment).

The difference between the estimated 3D motion field and the measured one was 3.3±3.6(5.4) mm and 3.8±3.1(5.8) mm (mean±std(95^{th} percentile)) for P01 and P02, respectively. Although statistical analysis showed a significant difference between the two motion fields (Wilcoxon test, α=5%), the 95^{th} percentile was similar to the maximum voxel size (i.e. 5mm). The difference in AP, RL and SI was quantified as 2.1±3.1(5.3) mm, 1.8±3.2(5.2) mm and 1.2±2.6(4.8) mm for P01 and 1.6±3.5(5.0) mm, 2.4±4.1(5.8) mm and 1.2±3.3(4.1) mm for P02.

4. Discussion

4.1. 4D CT lung XCAT phantom

For all the phantom cases, the proposed method provided an *estimated3D* volume close to *ground_truth*, showing potential of this approach to account for tumor motion and provide 3D data for in-room volumetric motion quantification.

It was anticipated that the selection of orthogonal sagittal and coronal slices centered in the tumor would mitigate the issue of out-of-plane motion, thanks to the robust description of SI and AP motion (i.e. main directions of respiratory motion) [15,16,17]. Nonetheless, we also tested the algorithm in presence of out-of-plane motion by simulating shifted slice positioning. In this scenario, results showed slightly higher errors with respect to a centered selection. However, the method was able to compensate for motion and errors were close to the voxel size (slice thickness of 1mm in the phantom). Considering a centered selection of cine-MRI in the tumor for patient data, it is expected that out-of-plane motion will have minimal impact with respect to the phantom, since patients are acquired with a 5mm slice thickness. The simulation with shifted slices, allowed also to evaluate non-rigid motion which can affect the correspondent slices between *cineMRI* and *pre-treatment3D*. With the advent of novel in-room MRI systems, where cine-MRI represents the state-of-the-art imaging modality for tumor tracking, it is expected that in-room 3D (or 4D) MRI are acquired just prior treatment, mitigating inter-fraction variations and providing a preliminary information of non-rigid motion for the definition of correspondent slices.

The method was also tested against existing alternatives from the literature. The proposed method was shown to perform better than the template matching approach, which assumes that there is no tumor shape change between the 3D template and the 2D slice image, thus compensating only for rigid motion [16], as visible in Figure 5. Better results in tumor motion compensation were achieved by the 3D reconstruction strategy with respect to the global motion model approach [20]. Unlike the global motion model approach, the proposed method does not rely on training data, which results in a reduced sensitivity to inter and intra-fraction variability. The 3D reconstruction method instead directly updates the pre-treatment volume including in the estimated volume the changes occurring during and between treatments via 2D DIR.

In terms of surrounding anatomy, errors in the 3D global reconstruction were higher far from the cine-MRI location with respect to results close to tumor location (Figure 4). This was mainly due to the lack of information for organs which were not included in the field of view of the cine-MRI, such as the heart (Figure 4). Another aspect was related to the fact that the motion field extrapolation along the RL and AP directions was a simple replication of the motion fields derived from 2D DIR, whereas the replicated SI direction was subsequently modulated by the two SI motion field components, featuring redundant information on both sagittal and coronal acquisitions. Our approach indeed assumed a correlation between the cine-MRI motion and the whole motion. This assumption is sufficiently valid in a neighborhood of the cine-MRI intersection (i.e. good compensation of non-rigid tumor motion), but limitations are still present in deriving the surrounding anatomy. As such the combination of our strategy with a motion model prior built on time-resolved images (i.e. 4DMRI) [21,22] could prove the optimal approach, providing a direct and accurate adaptation of tumor motion

thanks to the 3D reconstruction method, with the addition of a more reliable volume estimation far from the cine-MRI intersection provided by the prior.

Limitations of the XCAT phantom are linked to X-ray-based image content. Future work will be focused on testing the method with an MRI phantom able to simulate different MRI acquisitions.

4.2. Patient data

Application of the 3D reconstruction technique on patient data showed the feasibility of using this approach to reconstruct a 3D tumor volume from real time interleaved slices and the pre-treatment volume.

Results highlighted variability between the cine-MRI and the *measured3D* volume (*measured3D/cineMRI* in Table 4), which limited the accuracy of *measured3D* as ground truth and made direct comparison of *estimated3D* with *measured3D* difficult. The lack of a ground truth in patient data is due to the impossibility of acquiring 3D data in real-time. Therefore, the validation of the method on the phantom highlights the applicability of the 3D reconstruction method on clinical MRI-guided data.

Both patients showed a good match between *estimated3D* and *cineMRI* used to derive it (*estimated3D/cineMRI* in Table 4), both in terms of tumor and diaphragm. This suggests that our method is able to directly capture the intra-fraction variations occurring during respiratory motion, thus being able to describe the actual in-room 3D motion.

The difference between the estimated motion field and the measured motion field (i.e. derived from 3D DIR between *pre-treatment3D* and *measured3D*) was quantified in both patients with a mean value in each direction of about 2mm. The greater difference in AP and RL directions with respect to SI shows the limitations of the method in extrapolating a motion field in these directions.

The difference between the pre-treatment and the cine-MRI sequence and the presence of artifacts in cine-MRI slices (Figure 7) affected 2D registration and subsequent 3D reconstruction. As such, the ability to acquire similar MR sequences for both cine-MRI and pre-treatment volumes in future studies would enable more robust validation on patients.

5. Conclusion

A feasibility study on the reconstruction of a 3D volume directly from 2D orthogonal cine-MRI slices was carried out. Results showed the capability of the method to compensate for non-rigid tumor motion accurately where cine-MRI are centered, by providing an alternative to existing methods for on-line tumor motion compensation. The method also provides a preliminary estimation of the 3D global anatomy, although errors are still present far from cine-MRI location. Future improvements of the method will aim to integrate our approach with a motion model prior, thus increasing the accuracy of the method in the full 3D anatomy and allowing dose calculation and adaptation.

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Figure Legends

Figure 1. 3D reconstruction method with respect to existing literature (i.e. template matching and motion model approaches). Direct extrapolation of the 3D motion from in-room 2D cine-MRI for an MRI-guided treatment: this can be applied locally for non-rigid tumor tracking and additionally extended for a preliminary evaluation of the surrounding anatomy.

Figure 2. Workflow of the proposed 3D reconstruction method. (i) DIR of the coronal/sagittal slices of the pre-treatment 3D volume (*pre-treatment3D*) on the corresponding in-room coronal/sagittal cine-MRI slices (*cineMRI*). (ii) Extrapolation of the 3D motion field from the 2D motion field components derived from DIR. Straight arrows for the motion field components derived from DIR (yellow arrow for vf_{cor_RL}, violet arrow for vf_{sag_AP} and blue arrows for vf_{cor_SI} and vf_{sag_SI}), while dashed arrows represent the replication of the 2D DIR to all the slices with the modulation of the redundant SI component. (iii) Application of the estimated 3D motion field to the *pre-treatment3D* volume to obtain the *estimated3D* volume to compare (iv) with the *ground_truth* volume (*measured3D* for patients).

Figure 3. XCAT phantom results (16mm motion case). Overlap of the *estimated3D* volume (green) obtained with the 3D reconstruction method to the *ground_truth* with (B) the selection of cine-MRI slices centered in the tumor and (C) with a shifted selection of cine-MRI in the tumor to simulate out-of-plane motion. Yellow arrow indicates the tumor in the three views.

Figure 4. Estimated 3D motion field. First row, (A) overlap of the *estimated3D* (green) with the *ground_truth* (red) close to tumor location and (B) far from the tumor location (distance from the tumor location of [80,80,20]mm in axial, sagittal and coronal directions respectively). Second row: relevant 3D estimated motion field (green arrows) along axial, sagittal and coronal views. Third row: 3D ground truth motion field (red arrows). Fourth row: motion field difference (yellow arrows) between the estimated motion field and the ground truth motion field. (C) Motion field difference [mm] over three portions (i.e. region of interests) along the SI direction; orange lines represent cine-MRI locations.

Figure 5. Comparison with other methods near the tumor location (A) and far from tumor location (B). First raw: difference between *pre-treatment3D* and *ground_truth* to highlight the range of motion. Second raw: difference between the estimated volume derived via template matching and the *ground_truth*. Third raw: difference between the estimated volume derived via global motion model and the *ground_truth*. Fourth raw: difference between the estimated volume (*estimated3D*) derived via 3D reconstruction and the *ground_truth*. Yellow arrow indicates the tumor in the three views.

Figure 6. Patient P01 (left column) and Patient P02 (right column). (A) Overlap of the *pre-treatment3D* (green) and *measured3D* (red) phases to show range of motion. (B) Overlap of the *estimated3D* (green) volume obtained with the 3D reconstruction method to the *measured3D* (red) volume to show motion compensation. Image differences (grey levels) are also reported in the axial, sagittal and coronal views.

Figure 7. Inhale variability for P01: *cineMRI* (green) vs. *estimated3D* (red) in the first row and *cineMRI* (green) vs. *measured3D* (red) in the second row. (A) Overlap of the coronal view. (B) Overlap of the sagittal view. (C) Difference in the coronal view. (D) Difference in the sagittal view. Yellow arrows indicate the difference around the tumor.

Figures – see uploaded files

Tables

Table 1. A summary of the acquired and estimated MRI images used in this study to perform and investigate the 3D reconstruction method.

Image set	Dimensionality	Time of acquisition	Use
pre-treatment3D	3D	pre-treatment	3D image used to perform a 2D DIR with sagittal and coronal *cineMRI* slices to create *estimated3D*
cineMRI	2D	intra-treatment	Interleaved 2D coronal and sagittal slices acquired at inhale during treatment that registered with the *pre-treatment3D* corresponding slices create *estimated3D.*
estimated3D	3D	intra-treatment	3D image created with the 3D reconstruction method from the 2D *cineMRI* and *pre-treament3D* DIR. Compared with the *ground_truth* (*measured3D* for patients).
ground_truth (measured3D* for patients*)	3D	pre-treatment (to simulate intra-treatment)	3D image compared with *estimated3D*

Table 2. Distance (median ± interquartile range) between *estimated3D* and *ground_truth* for all the XCAT simulations in terms of Dice Coefficient, tumor COM distance [mm], diaphragm motion [mm] and landmark distance [mm].

estimated3D vs. ground_truth	3cm in SI centered slices	16mm/4mm in SI/AP centered slices	16mm/4mm in SI/AP shifted slices
Dice coefficient [a.u.]	0.9	0.9	0.8
COM distance [RL, AP, SI] mm	[0,0,1.5]	[0.1,0.5,1]	[0.1, 1.2, 1.5]
Diaphragm distance [mm]	2.4±2.6	1.3±2.3	1.7±3.1
Landmark distance [mm]	2.2±3.1	1.6±3.2	2.1±3.4

Table 3. Distance (median ± interquartile range) between the *ground_truth* and the derived volume with three different strategies (case of lung tumor with 16mm/4mm in SI/AP and centered cine-MRI slices) in terms of Dice Coefficient and tumor COM distance [mm], diaphragm motion [mm] and landmark distance [mm].

	Template matching	Global motion model	3D reconstruction
Dice coefficient [a.u.]	0.9	0.7	0.9
COM distance [RL, AP, SI] mm	[0.1,0.7,1.2]	[0.2,1.1,1.8]	[0.1,0.5,1]
Diaphragm distance [mm]	6.2±3.8	1.9±3.5	1.3±2.3
Landmark distance [mm]	4.0±4.2	1.2±1.4	1.6±3.2

Table 4. Patient quantitative results. Diaphragm distance and tumor parameters (Dice coefficient and COM distance). Highlighted in grey the accuracy of the *estimated3D* volume in describing the real in-room motion provided by *cineMRI*, which is not instead provided by *measured3D*.

	range of motion	***estimated3D/ measured3D***	***estimated3D / cineMRI***	***measured3D / cineMRI***
Patient P01				
Dice coefficient [a.u.]	0.7	0.6	0.9	0.6
COM distance [RL, AP, SI] mm	[2, 5.3, 1.5]	[0.8, 3, 2.5]	[0.3, 1.5, 0.8]	[0.8, 4.3, 1.5]
Diaphragm distance [mm]	10.6±3.5	4.7±2.4	2.5±1.9	2.9±2.0
Patient P02				
Dice coefficient [a.u.]	0.9	0.9	0.9	0.8
COM distance [RL, AP, SI] mm	[0.3, 1.5, 0.2]	[0.2, 1.5, 0.1]	[0.2, 1.5, 0.1]	[0.3, 1.8, 0.3]
Diaphragm distance [mm]	8.3±2.3	4.7±1.6	2.4±3.2	5.9±2.6