Original Research Article

The effect of respiration-induced target motion on 3D magnetic resonance images used to guide radiotherapy

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A B S T R A C T

Background and purpose: 3D Magnetic Resonance Imaging (MRI) is used in radiation therapy for reference planning and, lately, for adaptive treatments on MR accelerators. This study aimed to investigate the impact of different types of respiratory motion on the apparent target position and extent in such scans.

Materials and methods: An MRI motion phantom with a 30 mm diameter target was used to simulate cranial-caudal (CC) motion and imaged at an MR-Linac using a standard clinically released 3D T2w sequence. Scans were acquired for each combination of functions \( \sin(t) \), \( \sin^2(t) \) and \( \sin^{12}(t) \), peak-to-peak amplitudes (5, 10, 15 and 20 mm), and periods (4, 5 and 6 s). Furthermore, respiration CC motion patterns from two patients were used. Motion functions were shifted such that the time average target position would match a static reference scan at 0-position. The target was automatically identified in coronal and sagittal images using k-means clustering. The mean position and area of the target were calculated and compared to the reference scan.

Results: Artefacts increased with amplitude and depended on the motion type. \( \sin(t) \) and \( \sin^2(t) \) oscillations resulted in a blurring of the target, which led to an increased target area, while \( \sin^{12}(t) \) motion did not show significant changes in the target area. However, for the \( \sin^{12}(t) \) motion, the offset in apparent position was prominent, while that was not the case for the \( \sin(t) \) and \( \sin^2(t) \) motion. The patient respiration motion profiles showed similar trends.

Conclusions: In 3D MRI, target motion can change apparent tumour extent and apparent position. The changes increase with motion amplitude and depend on the motion type.

1. Introduction

Magnetic resonance imaging (MRI) is an indispensable imaging modality in external beam radiotherapy (RT). It has for decades been used for diagnostics and staging of cancer and is used as the standard of care within RT treatment planning in many cancer diagnoses [1]. Most recently, image-guided radiotherapy based on MRI has been enabled with the clinical introduction of systems combining an MRI scanner and a linear accelerator, known as MR-linacs [2,3]. The superior soft-tissue contrast of MRI compared to computed tomography (CT) images supports the delineation process and has been the driving incentive for MRI’s increasing use in RT [4], since target delineation is considered one of the major uncertainties within RT planning [5]. The introduction of online MR-guided treatments has therefore facilitated high-dose delivery to targets adjacent to sensitive organs at risk (OAR) in the abdomen, e.g. treatment of pancreatic tumours [6].

Unfortunately, MR images are prone to much more complex artefacts than those typically seen in CT [7]. Moreover, artefact types leading to geometrical misalignments have very different impacts on diagnostics and RT [8], which is reflected in the relatively few investigations on this topic within the radiology community. For example, in diagnostic imaging, an increased signal-to-noise ratio is typically prioritised over geometrical accuracy since the task is to detect possible malignancies rather than knowing their exact location [9]. For the same reason, if motion is present, it is much more important to acquire high-contrast images, e.g. by using gated acquisition, than to ensure that the tumour is imaged at the “mean” position. In RT, on the other hand, due to the high conformity of the planned doses, geometrical accuracy is critical to minimise the risk of under-dosage of the target and over-dosage of critical structures [10].
Magnetic resonance imaging (MRI) of targets in the abdomen is dominantly affected by the patient’s respiratory motion, leading to artefacts such as blurring and ghosting (discrete copies of the moving anatomy) [11], which increases the delineation uncertainty. Motion mitigation techniques such as breath-hold and shallow-breathing may reduce these artefacts [12], but lack of patient compliance or technical limitations of the equipment may preclude its use [13]. Even if beam-gating is available during dose delivery, it may not necessarily be the first choice since treatment delivery is substantially prolonged. 4D-MRI and cine imaging can quantify the motion and estimate proper ITV margins. Furthermore, 4D-MRI can be the basis for the mid-ventilation planning approach [14]. However, these are not standard approaches and are currently not readily available clinically. Furthermore, it might have limited accuracy as it only captures a limited period of the breathing pattern [15,16].

In a standard MR-linac workflow, 3D MRI is used for treatment planning, both in the preparation phase and at each treatment fraction for adaptation [17] in order to reduce the geometrical distortion. However, blurring and ghosting cannot be avoided in Cartesian read-out when motion is present [18,19]. Yet, the geometric accuracy of moving targets achieved with 3D MRI has so far not been investigated, although it is directly linked to the accuracy of the position of the delivered dose.

This study aimed to investigate how a moving target is visualised in a Cartesian 3D MRI by examining a moving target’s apparent position and extent on 3D T2w MRI. Different idealised but clinically relevant breathing patterns, as well as real patient breathing patterns, were analysed.

2. Material and methods

2.1. Motion phantom

An MRI-compatible motion phantom (Quasar MRI 4D-motion phantom, Modus Medical Devices, Ontario, Canada) was used to simulate respiratory motion. The static compartments of the phantom were filled with demineralised water. The moving part of the phantom consists of a cylinder (80 mm diameter) with a 30 mm sphere (the target) at the central axis, both filled with demineralised water (Fig. 1). Gadolinium-based contrast was added to the target sphere to create a contrast between the target and the surroundings.

2.2. Target motion patterns

The phantom motion software (Quasar Respiratory Motion, v. 4.1.19.20100) was used to program the phantom to perform specific respiratory motion patterns in the cranial-caudal (CC) direction. The motion patterns were mathematically defined or based on motion patterns from two previously treated patients (Fig. 2).

The mathematically defined functions were chosen as \( \sin(t) \), \( \sin^2(t) \) and \( \sin^{12}(t) \) to exemplify respiration cycles with different fractions of time in exhale position (Fig. 2 top). A 3D MRI was acquired for all combinations of function \( \sin(t) \), \( \sin^2(t) \) and \( \sin^{12}(t) \), peak-to-peak amplitudes \( A \) of 5, 10, 15 and 20 mm and periods \( T \) of 4, 5, and 6 s, which reflects typical respiration patterns seen in the clinic.

The tumor motion patterns from the patients were obtained from two patients treated for adrenal gland metastases. As described in supplementary material A, these motion patterns were extracted from existing intra-fractional cinématic MR images acquired at the Unity machine. Only the CC component of the patient target motion pattern was used, as this is the main direction for respiratory motion.

The patient’s motion patterns had comparable peak-to-peak amplitude (8.9 mm and 12 mm). One patient had a sin-like motion, while the other had a sin\(^{12}\)-like motion (Fig. 2 bottom). Geometrical errors related to larger amplitudes were investigated by acquiring two scans for each patient respiration curve, one with the original amplitude and one with the amplitude increased by 50%.

Reference scans were acquired while the phantom target was in the static central position (0-position) and shifted \( \pm 10 \) mm in the CC direction to verify the scale of the target movement. An offset was applied to all motion patterns such that the time average target position would match the central reference scan (0-position). Finally, the measurement uncertainty was evaluated by ten repetitions of the scan of the \( \sin(t) \), \( \sin^2(t) \) and \( \sin^{12}(t) \) oscillation with a peak-to-peak amplitude of 20 mm and a period of 5 s. The phantom was operated from the MR-linac control room. The phantom motion was started before each scan, without any specific timing between phantom and imaging start, to avoid amplifying possible synchronisation-related effects. The recorded patient target motion had a duration of 100 s and were therefore repeated for the duration of the scans.

2.3. MRI protocol

The phantom was imaged using the standard 3D T2w sequence settings for abdominal imaging on the Unity MR-linac (Elekta AB, Stockholm, Sweden). The phantom was aligned such that motion was in the Z-direction (along the table direction and parallel with the main magnetic field), i.e. orthogonal to the axial slice planes of the acquisition. Sequence details were as follows: Scan mode 3D with Turbo Spin Echo (TSE) parameters being repetition time (TR) 2100 ms, echo time (TE) 206 ms, flip angle (FA) 90 degrees, Echo Train Length (ETL) 134, matrix 448 (right-left (RL), read-out) \( \times 320 \) (anterior-posterior (AP)) \( \times 250 \) (CC), acquisition resolution 2 mm \( \times 2 \) mm, slice 2.4 mm, \(-1.2 \) mm gap, reconstruction resolution 0.56 mm \( \times 0.56 \) mm \( \times 1.2 \) mm. K-space sampling mode was Cartesian with linear order. Number of excitations (NEX) = 2. Parallel imaging was applied with SENSE factors 3.4 (RL) and 1.2 (FH). A 4-channel phased array anterior coil and a 4-channel phased array built-in posterior coil were used. Scan time per acquisition was 199 s.

2.4. Image analysis

For each scan, one central sagittal and coronal slice, close to the central stem holding the target, were analysed in MATLAB (Mathworks Inc., Natick, MA, USA). Segmentation of the target was automated using a five-level K-means-clustering of the grey values within the images [20]. The level related to the most hypo-intense region was defined to be the target. Within the images, the mean target position (the average pixel position of the region defined to be the target), and the target area (the number pixels defined to be the target), were extracted and compared to those of the 0-position reference scan. This procedure was performed for both the sagittal and coronal images; the reported values are the average of the two sets of values.
3. Results

All types of applied target motion introduced ghosting in the Z-direction. Changes in the apparent target area and position depended on the motion function, as illustrated in Fig. 3 (and supplementary material section B). For the mathematically defined oscillations, the \( \sin(t) \) and \( \sin^4(t) \) resulted in a blurred target, while \( \sin^{12}(t) \) motion led to a more well-defined target but with an offset in the apparent target position compared to the reference scan. Fig. 4 shows the apparent target area (top) and the apparent mean position (bottom) as a function of peak-to-peak amplitude. When present, both types of geometrical errors increased as a function of motion amplitude. The offset was the most prominent for the \( \sin^{12}(t) \) motion and grew to more than 3 mm for a peak-to-peak motion of 20 mm; however, for this motion pattern, only modest changes were observed in the area of the target. This was the opposite for the \( \sin(t) \) and \( \sin^4(t) \) functions, where a limited shift in apparent offset was seen while there was an increase by more than 40% in the apparent target area for 20 mm peak-to-peak motion. No clear correlation was observed between the investigated range of respiration periods and the apparent position and area. The same pattern was observed for the patient respiration curves (Fig. 3 bottom, and Fig. 4): The sin-like respiration did not result in a major offset in the target position, while an offset was present for the \( \sin^{12}(t) \) motion, which seemed to increase with increasing peak-to-peak amplitude. For the \( \sin(t) \), \( \sin^4(t) \) and \( \sin^{12}(t) \) motion with 20 mm peak-to-peak amplitude and 5 s period, the ten repeated scans resulted in a standard deviation (SD) in the measured offset of 0.9 mm, while the apparent target area had an SD ranging from 8 to 10 percentage points (errorbars shown in Fig. 4).

4. Discussion

For moving targets imaged using 3D Cartesian MRI, this study shows that both the apparent target extent and position offset depend on the motion pattern and the peak-to-peak motion amplitude. For symmetric target motion with comparable time in the exhale and inhale phase, i.e. a sin-like motion, the error in apparent position offset is small, while the apparent target area on the evaluated images increases with amplitude. For target motion with a large proportion of the respiratory cycle in the exhale phase, the error in the apparent target area is small, while a significant offset in the apparent target position is observed. Since breathing cycles often are characterised by a prolonged exhale phase [21], the offset will be present for many patients. Both types of geometrical errors have consequences when 3D Cartesian images are used to guide treatments, especially in the online adaptive setting. For peak-to-peak motion of 15 to 20 mm, the phantom study shows a 2–4 mm offset for \( \sin^{12}(t) \) like target motion. The effect of this offset is small for large targets treated with homogeneous dose distribution and wide margins. But for stereotactic body RT (SBRT) using inhomogeneous dose...
distribution, tight PTV margins, and small target volumes, the offset can introduce under-dosage in parts of the GTV and unintended high doses to surrounding critical normal tissue. In addition, the blurring artefact has a clinical impact since a larger volume than needed will be included as the target region leading to increased irradiation of healthy tissue. It is therefore important to know that these geometrical errors can be present and take them into account if needed.

A hand-waving argument might explain the observed geometrical errors. For the respiration pattern with a long time in the exhale phase (e.g. sin^{12}(t)), only a relatively small fraction of k-space is sampled in a position away from the exhale phase. Thus, the imaged target will resemble a static target in the exhale phase, resulting in sharp edges but offset from the mean position since most of the information is sampled in the exhale phase. On the contrary, when the respiration time is more evenly distributed within the respiration cycle (e.g. sin(t)), the k-space is sampled with positions evenly distributed above and below the mean position. This results in symmetrical blurring of the target but the target will be shown at the correct time-averaged mean position. The standard MRI sequence investigated used a linear read-out order of K-space, but other schemes, such as centre-out, are not expected to change the results since the reasoning above will still apply. Results similar to those presented in the article but for different sequences are supplied in supplementary material B.

Radial MRI, like VANE sequences (Philips Healthcare, Best, The Netherlands), is known to be relatively insensitive to motion insofar that noise from moving structures does not propagate as ghosts but is distributed more diffusively across the entire image. This may provide better images for viewing but will not remove the position-offset problem. However, the pattern of respiration introduced motion artefacts and geometrical errors for different motion types should be investigated for any sequence used for treatment guidance of moving targets.

In RT, three main approaches have been used for handling moving targets.
targets: beam gating, ITV-based planning supported by cinematic imaging, and mid-position reference planning based on 4D image acquisition [12]. The beam gating approach, supported by triggered (e.g. navigated) or breath-hold MR imaging for reference planning significantly increases delivery time due to the necessary multiple breath-holds. The ITV approach increases the treated volume and the dose delivered to surrounding OAR. The mid-position approach calculates an adequate PTV margin based on the motion amplitude. This results in slightly larger volumes than beam gating but is more robust to setup errors and supports efficient dose delivery without beam interrupts. However, 4D MRI and mid-position scan selection have not been commercially available in an MRL workflow. For MRL treatments without beam gating, the breathing movements should be reduced to a minimum, e.g. by using compression belts [22–24] and shallow breathing. A recent study on a Unity MR-linac demonstrated real-time aperture tracking based on cine imaging of the target during continuous treatment delivery [25]. Such development in treatment delivery will make it possible to use breath hold or navigated scans for plan adaptation without any increase in apparent target volume and compensate for any offsets in target position during delivery. Such implementation will reduce the uncertainties of MR-guided delivery without the use of breath-hold delivery and the related extensive beam-on times.

Detailed 4D analysis based on CT or MR in the pre-planning phase should be used to assess not only the motion amplitude but also the type of motion to predict the magnitude and type of introduced artefacts. Motion-free images, e.g. breath-hold images, in the pre-planning phase can be used to assess the volume and shape of the target. However, it is necessary to stress that both volume and shape can change during the respiration cycle and between treatment fractions due to radiation response and influence from surrounding tissue, e.g. changes in stomach shape. For targets in the lung, it has been shown that the overall peak-to-peak respiration amplitude is unchanged during a treatment course [26,27]. However, the inter- and intra-fractional stability of the motion type is yet to be investigated, and could change due to changes in patient relaxation and stress which can affect the ratio between exhale and inhale [21].

This study could have used other segmentation methods such as knowledge-based algorithms (e.g. AI models or contour propagation). But these would probably introduce a bias underestimating the apparent target area as these are based on prior knowledge of the true target shape. The k-means algorithm is not based on prior knowledge but is sensitive to small changes in image intensity. An example is shown in Fig. 3 for the sin12 motion, where the eye would have made another segmentation of the expected spherical target compared to the K-means algorithm.

The uncertainty assessment of the measurements was made for the mathematically defined motion patterns with peak-to-peak motions of 20 mm and periods of 5 s. The uncertainty was almost identical for the three different motions despite the sin motion generated the highest level of blurring and aliasing artefacts. The uncertainties reported in a phantom study with an automated target delineation does clearly not reflect the uncertainty in daily clinical practice, which will include uncertainty related to additional noise and subjective target delineation. The present study only investigated motion in the CC direction, as this is the most dominant respiratory motion. In addition, the data are based on regular periodic motion, except for the patient target motion data. Similar measurements with irregular and non-periodic target motion in multiple directions will likely modify the observed effects somewhat and could warrant further investigations. However, the main effects observed in this study are expected to be present, particularly the offset artefact.
In conclusion, target motion can change apparent extent and position relative to the average tumour position in Cartesian 3D T2w MRI. These changes are linked directly to the range of the motion and respiration pattern (fraction of time in the exhale phase). Thus to ensure that “what you see is what you treat”, target motion should be reduced as much as possible. 4D imaging should be used not only to measure the peak-to-peak motion amplitude but also to assess the type of motion to be able to predict the magnitude and type of introduced artefacts and to consider their clinical impact. In addition, it is recommended that respiratory-induced motion artefacts are assessed for any Cartesian or Radial 3D MRI sequence that is used to guide radiotherapy.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could appear to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.phro.2022.11.010.

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