Simultaneous motion monitoring and truth-in-delivery analysis imaging framework for MR-guided radiotherapy

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Abstract

Intrafraction motion (i.e. motion occurring during a treatment session) can play a pivotal role in the success of abdominal and thoracic radiation therapy. Hybrid magnetic resonance-guided radiotherapy (MR-gRT) systems have the potential to control for intrafraction motion. Recently, we introduced an MRI sequence capable of acquiring real-time cine imaging in two orthogonal planes (SOPI). We extend SOPI here to permit dynamic updating of slice positions in one-plane while keeping the other plane position fixed. In this implementation, cine images from the static plane are used for motion monitoring and as image navigators to sort stepped images in the other plane, producing dynamic 4D image volumes for use in dose reconstruction. A custom 3D-printed target, designed to mimic the pancreas and duodenum and filled with radiochromic FXG gel, was interfaced to the dynamic motion phantom. 4D-SOPI was acquired in a dynamic motion phantom driven by an actual patient respiratory waveform displaying amplitude/frequency variations and drifting and in a healthy volunteer. Unique 4D-MRI epochs were reconstructed from a time series of phantom motion. Dose from a static 4 cm × 15 cm field was calculated on each 4D respiratory phase bin and epoch image, scaled by the time spent in each bin, and then rigidly accumulated. The phantom was then positioned on an Elekta MR-Linac and irradiated while moving. Following irradiation, actual dose deposited to the FXG gel was determined by applying a $R_1$ versus dose calibration curve to $R_1$ maps of the phantom. The 4D-SOPI cine images produced a respiratory motion navigator that was highly correlated with the actual phantom motion (CC = 0.9981). The mean difference between the accumulated and measured dose inside the target was 4.4% of the maximum prescribed dose. These initial results demonstrate that 4D-SOPI is a promising imaging framework enabling simultaneous real-time motion monitoring and truth-in-delivery analysis for integrated MR-gRT systems.

Introduction

Intrafraction motion (i.e. motion occurring during a treatment session) can play a pivotal role in the success of abdominal and thoracic radiation therapy. With the steep dose gradients typically employed to reduce doses to proximal organs at risk (OAR), large and dynamic translations, rotations, and deformations arising from respiration, peristalsis, organ filling, drifting, or bulk motion can compromise target coverage and obscure OAR doses (Goldstein et al 2010). Although a number of methods to monitor intrafraction motion (Mageras et al 2001, McBain et al 2009) and reduce its severity (Kubo and Hill 1996, Keall et al 2001, Trofimov et al 2008) have been introduced, imaging frameworks that support intrafraction motion management and ‘truth-in-delivery’ analysis (i.e. dose reconstruction) are still under development.

Hybrid magnetic resonance-guided radiotherapy (MR-gRT) systems (Fallone 2014, Keall et al 2014, Lagendijk et al 2014, Mutic and Dempsey 2014) permit non-ionizing, high soft tissue contrast imaging before
(pre-beam), during (beam-on), and after (post-beam) radiotherapy delivery. With its high temporal resolution, two-dimensional (2D) cine MRI is a natural choice for continuous, real-time, intrafraction motion monitoring during beam-on. However, even with the use of simultaneous multi-slice (SMS) excitation, cine MRI is only capable of imaging a limited number of 2D slices, which limits its utility for dose calculation.

Four-dimensional (4D) MRI is capable of constructing volumetric (3D) images correlated with specific structure motion or motion surrogates. A plethora of 4D-MRI methods have been introduced, including prospective and retrospective multi-slice 2D (Hu et al 2013, Tryggestad et al 2013, Celicanin et al 2015, Freedman et al 2017, Breuer et al 2018) and retrospective 3D approaches (Deng et al 2016, Han et al 2017, Rank et al 2017). Although 4D-MRI can resolve motion in three dimensions, several motion cycles are required to meet the data sufficiency conditions to construct 4D volumes. This limits the utility of 4D-MRI for real-time intrafraction motion monitoring.

Recently, the combination of pre-beam 4D-MRI and beam-on cine imaging has been proposed as a dose reconstruction imaging framework for hybrid MR-gRT systems. In this approach, a motion model generated from the 4D-MRI is dynamically updated throughout the treatment fraction through deformable image registration (DIR) with the cine images (Stemkens et al 2016, 2017). The dynamic update of the motion model facilitates generation of a synthetic 3D volume at the temporal frame rate of the cine images, while also permitting control for deviations from the average respiratory cycle determined from the pre-beam 4D-MRI. Such a method, while promising, depends on DIR at two points during the dose accumulation process. First, DIR is required to calculate the intrafraction volumes. Second, DIR is required to warp the doses calculated on each phase to a reference phase for accumulation. While the second DIR step may not be avoided, a method to eliminate the DIR dependence during construction of intrafraction volumes may be desired.

If the use of DIR is to be avoided when computing intrafraction volumes, dynamically updating 4D-MRIs must be reconstructed throughout the treatment fraction. A straightforward approach would be to acquire continuous 3D data (e.g. golden angle radial stack-of-stars Feng et al (2015)) during beam-on and retrospectively reconstruct 4D-MRI epochs that account for short-term variations in respiratory pattern or physiological effects such as organ filling. However, the ability to acquire real-time images for intrafraction motion management (e.g. gating, tracking, trailing) is lost with this approach.

Recently, we introduced a method capable of acquiring real-time cine MR images from slices in orthogonal planes simultaneously (SOPI) (Mickevicius and Paulson 2017b). By performing sequential excitation and simultaneous phase encoding of orthogonal slices, signals originating from packets of SMS slices within orthogonal planes can be acquired within the same repetition time (TR). Simultaneous image refocusing (SIR) and/or parallel imaging methods can then be used to separate the simultaneously excited slices.

In this work we extend the SOPI method to enable simultaneous real-time motion monitoring and construction of dynamic, self-navigated 4D-MRI epochs within an MR-gRT treatment fraction. The goals of the present work were three-fold. First, test the ability of 4D-SOPI to acquire respiratory phase-resolved 4D-MRI volumes in a dynamic motion phantom and in vivo. Secondly, test the ability of 4D-SOPI to reconstruct serial, self-navigated 4D-MRI epochs throughout a scan duration consistent with the length of an intensity modulated radiotherapy (IMRT) treatment fraction. To differentiate between the serial 4D-MRI datasets, the authors chose the word ‘epoch’ since it nicely describes the subdivision of the 4D-MRI acquisition into multiple time periods. Finally, test and validate the use of 4D-SOPI for dose reconstruction in a dynamic motion phantom.

**Methods**

**Pulse sequence**

Two variations of the 4D-SOPI pulse sequence were implemented. The use of an SMS factor of two was used in the imaging slice group throughout this study. The first variant, referred to as one-plane 4D-SOPI (1PL-4D-SOPI), acquires a cine navigator slice in one orthogonal plane while stepping through groups of SMS imaging slices in the second orthogonal slice plane. The two-plane variation (2PL-4D-SOPI) acquires one cine navigator slice in each of the orthogonal planes while acquiring a single imaging slice at a time. These two sequence variants are depicted in figure 1.

The pulse sequence timing diagram for 4D-SOPI is shown in figure 2. It is based on the previously published nETE SOPI sequence (Mickevicius and Paulson 2017b). The slice-select axis of one slice group lies on the phase encoding axis of the other. Both orthogonal slice groups share a frequency encoding direction. In this study, the first RF pulse played out within each TR corresponds to the navigator slice which is orthogonal to the 4D imaging slices. The second RF pulse is a multiband pulse which excites two slices in the 4D imaging plane simultaneously. To spatially encode these slice groups simultaneously, gradient lobe areas must be calculated based on the area of the current phase encoding gradient area, $P$. The expressions to calculate these areas are as follows:

\[ B = -A_2 - P \]  \hspace{1cm} (1)
With the above expressions for the frequency encoding prephaser gradients, \( F \) and \( G \), the use of an extended frequency encoding gradient can be used to separate the signals from the orthogonal slice groups according to the

\[
E = -D_2 \\
C = -D_1 + P \\
F = -I \\
G = -H. 
\]
SIR principle. The aliased signals from the SMS slices remain entangled within the gradient echo corresponding to the 4D imaging slice packet.

The RF pulses were implemented as phase-tagged sinc pulses with duration 0.6 ms and bandwidth 2 kHz. Phase tags were used to apply CAIPIRINHA phase ramps to achieve a FOV/2 shift between simultaneously excited slices within the 4D imaging plane. Additionally, the SMS slices were excited in quadrature to avoid interference and to facilitate a phase constrained reconstruction. To accelerate the acquisition of each frame, an in-plane reduction $R = 3$ and 5/8 partial Fourier were used.

**Image reconstruction**

To reconstruct the navigator images for the 1PL-4D-SOPI acquisition, a GRAPPA interpolation kernel was calculated from fully sampled autocalibrating signal (ACS) lines near the center of $k$-space. This kernel was used to interpolate the skipped phase encoding lines. Subsequently, a homodyne partial Fourier algorithm was used to restore the conjugate symmetric portion of $k$-space.

A phase constrained 2D-SENSE-GRAPPA algorithm was used to separate signals from simultaneously excited slices in the 4D imaging slice group. This kernel was calculated from a low-resolution calibration scan. The kernel is applied to the undersampled portions of the $k$-space of an extended readout FOV representation of the SMS slices. The virtual conjugate coil (VCC) method was used to exploit the phase differences between the SMS slices (Blaimer et al 2009). The same homodyne reconstruction algorithm was used to restore the conjugate symmetric portion of $k$-space of each SMS slice. The details of the algorithm implementation have been previously described (Mickevicius and Paulson 2017b).

**Self-navigated 4D image sorting**

An intensity projection through a high-contrast tissue interface was extracted directly from the cine images and plotted over time. The center of mass of the intensity projection was calculated in each frame to produce a 1D motion surrogate signal, which was used to sort the imaging slices into respiratory phase bins. For each desired 4D-MRI epoch, the motion surrogate was placed into one of four-to-six respiratory bins based on the amplitude of the 1D signal. Within each epoch, the peak-to-peak amplitude of the surrogate was divided equally into the number of bins. The relatively small number of respiratory phases reconstructed was chosen to simplify the workflow to perform the subsequent dose reconstruction. The imaging slices acquired concurrently with each frame of the navigator slice were placed into the corresponding respiratory phase. Repeat images within each bin were averaged.

**Phantom target**

A custom phantom mimicking the pancreas and duodenum was designed and 3D-printed with PLA filament (see figure 3). The pancreas and duodenal structures of the phantom were filled with radiochromic FXG (Fricke xylene orange) gel (Lee et al 2018). This combination of filament and gel was chosen due to their tissue-equivalent and radiological properties (Keall and Baldock 1999, Ehler et al 2014, Burleson et al 2015, Jeong et al 2015, Craft and Howell 2017, Craft et al 2018). An air-filled cavity within the duodenum was incorporated in the phantom design to induce the electron return effect at the duodenal wall during irradiation on a prototype Eleka MR-Linac (Elekta Instruments AB, Stockholm, Sweden) with orthogonal magnetic and irradiation fields. The 3D-printed target was interfaced to a dynamic MRI-compatible motion phantom (Model 008M, CIRS, Norfolk, MA).

**Phantom experiment**

The respiratory surrogate waveform extracted from a Varian RPM system during 4D-CT imaging of a pancreas patient is shown in figure 4. The time duration of the waveform was 7.5 min. The waveform was used to drive the dynamic motion phantom in the superior-inferior direction. Dynamic motion phantom images from a 1PL-4D-SOPI Fast Imaging with Steady Precession (FISP) scan were acquired on a Siemens 3T Verio scanner (Siemens Healthineers, Erlangen, Germany) with 21 receive coils. A single sagittal navigator slice and 62 coronal slices with a thickness of 3 mm were prescribed. The $TE_1/TE_2/TR$ from the scan were 3.5/1.5/5.3 ms, respectively. A flip angle of 20° was prescribed. The FOV and matrix size were 340 mm and 128 × 128. A reduction factor of three ($R = 3$) and 5/8 partial Fourier were used for in-plane acceleration. With 48 phase encode lines per frame, the total amount of time to acquire $k$-space data for an SMS = 2 pair of coronal slices and sagittal navigator slice was approximately 0.25 s (four frames per second). Three 4D-MRI epochs with five bins were reconstructed, each using a sequential 1/3 of the data. Three epochs were chosen since the range of motion surrogate signal amplitudes within each epoch was approximately equal. A brief, low-resolution single-band calibration scan was performed to calibrate the 2D-SENSE-GRAPPA interpolation kernels prior to 4D-SOPI acquisition.
An *in vitro* dose reconstruction experiment simulating a hypofractionated pancreas cancer MR-gRT fraction on a prototype Elekta MR-Linac was performed. Fifteen reconstructed 3D volumes of the dynamic motion phantom, obtained from the 1PL-4D-SOPI acquisition described above (5 bins per 4D epoch; 3 total 4D epochs), were resampled to 1 mm cubic voxels and then loaded into a research version of the Monaco treatment planning system (TPS) (v5.19.03.03d, Elekta Instruments AB, Stockholm, Sweden). Electron densities of each phantom structure were determined from a prior CT scan of the phantom (Definition AS Open, Siemens Healthineers, Erlangen, Germany). Subsequently, bulk electron density assignment of each structure within the phantom and target was performed in Monaco. For each of the fifteen volumes, dose from a single 4 cm × 15 cm static open field oriented at gantry = 0° was calculated using a 2 mm grid spacing and 1% statistical uncertainty per control point. The effects of the MR-Linac cryostat and presence of the transverse 1.5 T magnetic field were incorporated during dose calculation. During this process, the position of the beam was kept fixed relative to the static components of the phantom (i.e. the phantom target was at different positions relative to the treatment field according to 4D bin and epoch number). At the nominal MR-Linac output of 432 MU min⁻¹, approximately 3200 MU were required for continuous irradiation over the 7.5 min duration of the respiratory waveform shown in figure 4. The relative monitor units (MU) used for dose calculation of each 4D bin and epoch were determined based on the fraction of time the phantom spent in each bin and epoch, shown in table 1.

The Monaco TPS was set to deliver 1 cGy/MU to water at 10 cm depth and 143.5 cm source-to-axis distance. However, the absolute calibration of the MR-Linac at the same position in water was measured to be 0.8766 cGy/MU at the time of the experiment. Therefore, the doses for each bin and epoch were scaled by 0.8766 to account...
for the difference between TPS and actual absolute dose. The scaled doses from all fifteen treatment plans were then sent to MIM (v6.7.6, MIM Software, Cleveland, OH). Local rigid registration was performed to align the targets of each 4D bin and epoch to the reference target position of bin 5, epoch 3. After registration, doses were consecutively summed to construct an accumulated dose.

The dynamic motion phantom was then positioned on the MR-Linac. The phantom motion was driven with the identical motion waveform used for the 1PL-4D-SOPI acquisition (i.e. figure 4) and simultaneously irradiated using a static 4 cm $\times$ 15 cm field with 3200 MU. Following irradiation, the phantom motion was suspended and quantitative spin-lattice relaxation rate ($R_1$) mapping of the dynamic motion phantom and target was performed using DESPOT1 (Deoni et al 2005) with five flip angles (3, 6, 10, 20, 30°) and TR = 20 ms (Schabel and Parker 2008). The 3D $R_1$ map was converted to absolute dose by applying a calibration curve obtained from a calibration experiment in which ten tubes of FXG gel were individually placed in a solid water phantom at $d_{max}$, 100 cm source-to-axis distance, and irradiated to known radiation doses ranging linearly from 0 to 4000 cGy on a Elekta Infinity linac using a 10 cm $\times$ 10 cm field size. The measured, absolute 3D dose distribution of the phantom was then compared against the accumulated dose distribution reconstructed in MIM.

**In vivo experiment**

Identical timing and resolution parameters as those used in the phantom experiment were also used to acquire 1PL-4D-SOPI FISP data in the abdomen of a consenting healthy volunteer on a Siemens 3T Verio scanner. Four 4D-MRI epochs of four bins were reconstructed for this scan. Additionally, a brief 2PL-4D-SOPI scan was acquired, and a single volume was reconstructed. The same calibration scan as in the phantom experiment was performed prior to acquisition of 4D-SOPI.

**Results**

An example sagittal navigator image from the phantom experiment is shown in figure 5 (a). An intensity projection was extracted from the wall of the target and was plotted over time. The projection and extracted respiratory motion waveform are shown in figure 5 (b). The respiratory motion navigator was highly correlated with the actual phantom motion (correlation coefficient = 0.9981). Partial saturation of the current and previous coronal slice groups is apparent within the navigator image in figure 5 (a).

Sagittal reformats of end-inspiratory phase images for each of three 4D-MRI epochs obtained in the phantom experiment are shown in figure 6. The red reference lines aid in visualizing the differences in target position between the different epochs. As expected, the target position in each of the end-inspiratory epochs differed along the superior / inferior direction due to the drift in the motion waveform used to drive the phantom. Slight slice mismatch within the end-inspiratory phase for each epoch is observed.

Figure 7 displays the relationship between spin-lattice relaxation rate, $R_1$, $(1/T_1)$ and absolute dose for the FXG gel at 1.5 T, determined during the calibration experiment. The $R_1$ versus absorbed dose line of best fit is shown in figure 7. Here, the dose in cGy is calculated using the longitudinal relaxation rate in units of s$^{-1}$. The $R^2$ value of linear fit was 0.995.

Following the calibration experiment, the relationship between absorbed dose and $R_1$ was applied to the 3D $R_1$ map acquired on the irradiated phantom. The 3D dose distribution measured via the FXG gel and the reconstructed dose calculated in MIM are shown in figure 8. The mean difference between reconstructed and measured dose inside the pancreas and duodenum phantom was 4.4% of the maximum prescribed dose. The localized dose increases at the air-duodenum interface arising from the electron return effect are apparent in both the reconstructed and measured dose distributions. In addition, similar smearing of the dose distributions along the superior/inferior direction due to motion is apparent.

An example in vivo sagittal navigator image of a healthy volunteer is shown in figure 9 (a). Due to the high levels of acceleration, the image has a relatively low signal-to-noise ratio. However, sufficient contrast is present to visualize the liver and kidneys, and to extract a respiratory waveform to be used for data sorting.

| Fraction of total MU | Epoch 1 | Epoch 2 | Epoch 3 |
|----------------------|---------|---------|---------|
| Bin 1                | 0.0167  | 0.0070  | 0.0113  |
| Bin 2                | 0.0376  | 0.0199  | 0.0355  |
| Bin 3                | 0.0774  | 0.0806  | 0.0538  |
| Bin 4                | 0.1059  | 0.1043  | 0.1898  |
| Bin 5                | 0.0957  | 0.1215  | 0.0430  |

**Table 1.** Fractions of time spent in each 4D-MRI bin and epoch used to determine the fraction of planned 3200 MU to apply to each 4D imaging bin and epoch during dose calculation.
A sagittal reformat of end-inspiratory phase images of each of the four 4D-MRI epochs for the 1PL-4D-SOPI volunteer scan are shown in figure 10. In this volunteer, the peak position of the liver at the end-of-inspiration remained relatively constant throughout all epochs, as demarcated by the red reference line. Visually, there is enough contrast in the images to delineate the liver and right kidney. In figure 11, end-inspiratory and end-expiration phase images from the first 4D-MRI epoch are shown.

**Discussion**

We introduced here a new imaging framework for intrafraction motion management in MR-gRT based on the simultaneous orthogonal plane imaging (SOPI) pulse sequence. The primary advantage of 4D-SOPI for MR-gRT is that it supports simultaneous prospective real-time cine imaging for intrafraction motion management (e.g. breath hold, gating, tracking, trailing) plus retrospective construction of serial, self-navigated, respiratory-correlated 4D volumes without relying on DIR.

With 4D-SOPI, DIR algorithms are not required to construct dynamic volumetric images for dose reconstruction. The construction of serial 4D volumes throughout a treatment fraction permits the 4D-SOPI method to resolve intrafraction motions arising from respiration, organ filling, drifting (e.g. due to muscle relaxation), and bulk motion. Although DIR algorithms are not required for serial 4D-MRI construction with 4D-SOPI, accumulation of reconstructed dose to a reference phase will still require DIR.
Differences in frequency and directionality challenge the simultaneous resolution of respiratory and peristaltic motions in the abdomen. 4D-SOPI is capable of handling these motions simultaneously through prescription of a coronal navigator slice, which permits self-navigated 4D-MRI reconstruction for dose reconstruction, and enables real-time intrafraction motion management strategies (e.g. gating, tracking) to control for peristaltic motions.

4D-SOPI permits several permutations of navigator and imaging slice geometries. One or more navigator slices can be acquired individually, orthogonally, or in parallel depending on the application. For example, parallel navigator slices could be positioned over the diaphragm and tumor or OAR. The diaphragm slice could be used for image-based, self-navigated 4D-MRI reconstruction while the tumor/OAR slice could be used to gate the radiation delivery. Alternatively, orthogonal navigator slices could be positioned to intersect a tumor or OAR.

Figure 7. Calibration curve relating absolute dose of FXG gel to longitudinal relaxation rate ($R_1$) at 1.5 T demonstrates a linear relationship. The equation to characterize the relationship between the relaxation rate ($R_1$) in units of s$^{-1}$ and dose in cGy is displayed on the figure.

Figure 8. Measured 3D dose distributions obtained via $R_1$ mapping of FXG gel in treated 3D-printed target of dynamic motion phantom (top row) demonstrates good agreement to reconstructed dose (bottom row). Focal dose hot spots due to the electron return effect are observable at the pancreas-duodenum interface.
Similarly, one or more imaging slices can be acquired individually, orthogonally, or in parallel. This unique flexibility also offers the potential to utilize super-resolution 4D-MRI reconstructions (Plenge et al 2012, Van Reeth et al 2015) with 4D-SOPI, which is an avenue of future exploration.

4D-SOPI offers some flexibility in the contrast of the acquired images. Contrast from any gradient spoiled pulse sequence (e.g. FLASH, FISP, PSIF) can be obtained depending on the desired contrast of the target. Furthermore, when employing the non-equal echo time (nETE) variant of SOPI, the effective TE of the navigator and imaging slice groups can be swapped by changing the order of excitation, thus providing additional control over contrast. This flexibility in image contrast can be exploited to improve the accuracy of DIR for use in dose accumulation or contour propagation in motion management strategies. Although interleaved orthogonal SMS cine imaging (an approach more straightforward to implement) could be considered as an alternative to SOPI, delays between the acquisition of the each sequential navigator frame and imaging slice could cause errors in the binning process during the retrospective 4D-MRI reconstruction. SOPI eliminates this potential uncertainty by acquiring time-locked navigator and imaging slices.

Validation of 4D-MRI has long been a challenge. One validation approach compares motion estimates from 4D-MRI against separate cine MRI acquisitions (Deng et al 2016, Han et al 2017). Another potential advantage of 4D-SOPI for 4D-MRI may be self-validation. Average motion contained within the navigator slice can be used to validate motion of the 4D-MRI epoch obtained over the same time period, in the same acquisition. This will a topic of future exploration.

As seen by slice mismatch in both the phantom and in vivo images, small variations in the motion state exist within each 4D-MRI bin. Using more bins would reduce this effect at the expense of requiring the interpolation of more slices that were not filled in each bin. As currently implemented, the image sorting takes place after obtaining magnitude coil-combined images. A potential improvement in image quality could be obtained by performing complex averaging of slices in the same location shuffled into the same bins. The impact of the slice mismatch on the accuracy of accumulated dose will be the topic of future investigations.

Partial saturation bands within each imaging plane are visible due to the intersection of the orthogonal slice groups. In this study, these bands did not impact the accuracy of dose accumulation since electron densities were forced in the phantom. An alternative approach may be to register a CT (or synthetic CT) to each respiratory phase prior to calculating dose. In this case the impact of the saturation bands is also expected to be small for mutual information or intensity-based registrations, but this effect should be thoroughly studied in future work.

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**Figure 9.** Results from in vivo study in a healthy volunteer. Example sagittal navigator image (a) and respiratory motion waveform (red time series in (b)) extracted from an intensity projection (red line in (a)) placed in the liver.

**Figure 10.** Sagittal reformatting of the end-of-inspiration phase for each of the four 4D-MRI epochs from the 1PL-4D-SOPI volunteer scan.
The 4D-SOPI method draws some similarity to a recently introduced 4D-MRI method that utilizes parallel imaging with controlled aliasing (CAIPIRINHA) to separate simultaneously acquired data from a sagittal navigator slice and a sagittal imaging slice (Celicanin et al 2015). However, through the use of SOPI and multiband pulses, 4D-SOPI provides more flexibility in navigator and imaging slice prescriptions.

It may be tempting to consider using the 4D-SOPI method to construct motion models for use in treatment planning (i.e. during MR simulation). While this is a possibility, higher quality 4D-MR images may be obtained with dedicated 3D approaches in shorter scan durations (Rank et al 2017, Mickevicius and Paulson 2017a). The main benefit of 4D-SOPI is the simultaneous real-time imaging and construction of serial, self-navigated 4D-MR epochs for dose reconstruction for abdominal and thoracic MR-gRT.

There are a few limitations of this study. First, quantitative comparison of accumulated and measured 3D dose distributions by Gamma analysis was challenged due to Gibbs ringing in the 3D $R_1$ maps (see figure 8). Though collection of higher resolution DESPOT1 images would rectify this issue, lower resolution $R_1$ mapping was performed to image faster, minimize fading of the FXG gel during measurement. Second, a simple beam model was chosen to validate the use of the 4D-SOPI for dose reconstruction. The relative length of the treatment fraction spent in each of the phases within each of the 4D-MRI epochs was used to weight the dose calculated on each respective 3D volume. For more complicated treatments (e.g. step-and-shoot or rotational IMRT), this simple linear weighting will not be accurate. Third, the target (pancreas) and OAR (duodenum) in the phantom study were rigidly connected. In vivo, a rigid target-based alignment will not be sufficient for accumulation of dose. Deformable image registration will be required to warp the dose maps to a reference phase following dose reconstruction. While the accuracy of real-time motion tracking estimates obtained with SOPI has been established (Mickeyvicius and Paulson 2017b), an in vitro experiment simulating complex motions observed in vivo would be difficult to perform. As an alternative, an in silico study using the 4D XCAT phantom (Segars et al 2010) will be used to provide quantitative metrics of 3D image and dose reconstruction accuracy in the presence of complex 3D non-rigid motions. Finally, the ‘intrafraction’ motion of the phantom was calculated on a separate MRI scanner from the MR-Linac, due to inaccessibility of the MR-Linac sequence development environment. Future work will implement the proposed imaging methodology on the Elekta MR-Linac, which will eliminate setup uncertainties associated with moving the motion phantom between systems and timing delays between the start of the motion and the start of the imaging/irradiation.

**Conclusion**

4D-SOPI is capable of providing simultaneous prospective real-time cine imaging for intrafraction motion management (e.g. breath hold, gating, tracking, trailing) along with retrospective construction of serial, self-navigated, respiratory-correlated 4D volumes for dose reconstruction. Initial results demonstrate that 4D-SOPI is a promising imaging framework for truth-in-delivery analysis in MR-gRT.

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