Fast cine-magnetic resonance imaging point tracking for prostate cancer radiation therapy planning

J Dowling¹, K Dang², Chris D Fox³, S. Chandra¹, Suki Gill², T. Kron², D. Pham², F. Foroudi²
¹CSIRO Australian e-Health Research Centre, Royal Brisbane and Women’s Hospital, Australia
²Peter MacCallum Cancer Centre, Melbourne, Australia

E-mail: jason.dowling@csiro.au

Abstract. The analysis of intra-fraction organ motion is important for improving the precision of radiation therapy treatment delivery. One method to quantify this motion is for one or more observers to manually identify anatomic points of interest (POIs) on each slice of a cine-MRI sequence. However this is labour intensive and inter- and intra-observer variation can introduce uncertainty. In this paper a fast method for non-rigid registration based point tracking in cine-MRI sagittal and coronal series is described which identifies POIs in 0.98 seconds per sagittal slice and 1.35 seconds per coronal slice. The manual and automatic points were highly correlated ($r>0.99$, $p<0.001$) for all organs and the difference generally less than 1mm. For prostate planning peristalsis and rectal gas can result in unpredictable out of plane motion, suggesting the results may require manual verification.

1. Introduction
Organ motion is an important factor in radiation therapy treatment, which aims to precisely deliver radiation dose to a target while limiting the amount of radiation to organs at risk. In prostate treatment planning the patient’s clinical target volume (CTV) is expanded with an internal margin covering potential intra-fraction organ movement to generate the Internal Planning Volume (IPV). An addition margin is then added for patient setup error to generate the planning target volume (PTV). The internal margin is necessary as during treatment the prostate and seminal vesicles can still move independently. Understanding the internal motion during each treatment delivery fraction is important to ensure that the intended and actual dose is the same.

Inclusion of the seminal vesicles in the CTV significantly increase the risk of acute and late rectal toxicity (1). Although a number of papers evaluate prostate motion during treatment less research has focused on seminal vesicle movement. This has motivated a clinical trial at the Peter MacCallum Cancer Centre, Melbourne, Australia, which aims to measure appropriate CTV to PTV treatment margins for the prostate and seminal vesicles based on cine-MRI point displacement data over a typical image guided radiation therapy treatment duration (15 minutes).

¹ To whom any correspondence should be addressed.
The traditional method for quantifying motion from these scans is for one or more expert observer to manually identify points of interest (POIs) on each slice (2,3). However this manual process is labour intensive and inter- and intra-observer variation can introduce uncertainty. This paper evaluates the use of fast deformable registration to map an initial set of points over the set of entire set of cine-MRI images.

2. Method

2.1.1. Image data
For this study cine-MRI scans were acquired prior to treatment for five patients prescribed radical radiation therapy to a dose of 78 Gy in 39 fractions using 3DCRT or IMRT techniques. Patients were advised to apply the same bowel and bladder preparation as for treatment (patients were asked to empty both bladder and bowels 30 minutes before treatment and then drink four small cups of water. Scanning commenced 30 minutes after the last cup of water). Patients were scanned in the treatment position on a flat table with the same stabilization devices as during treatment.

The Cine-MRI datasets were acquired with a true-FISP T2w sequence on a Siemens 3T Tim Trio. 2D images were stored at four second intervals along sagittal (n=235, size=416x512 pixels, total time=940 seconds) and coronal (n=200, size=512x512 pixels, total time=800 seconds) planes. The total scan time each session was 30 minutes (15 minutes for the sagittal followed by 12 minutes for the coronal plane).

2.1.2. Manual point collection
Manual points were carefully marked on each cine-MRI series by an experienced radiation therapist using custom in-house software which recorded the name and co-ordinates of each point. The points of interest marked are shown in Figure 1 and were used for to calculate the displacement of either the organ centroid (C) or the absolute position (A) of a landmark. For the sagittal images the points comprised the bladder (C), prostate (C), seminal vesicles (C), rectum (C), pubis symphysis (C), and external surface marker (A) and the anterior edge of the coccyx (A). For the coronal images the points consisted of the bladder (C), prostate (C), right and left seminal vesicles (C) and right and left femoral head (A).

![Figure 1. Sagittal (left) and Coronal (right) initial slices with points overlaid for study patient #2 (points have been enlarged for visibility in this paper)](image_url)
2.1.3. Automatic point tracking

The aim of the automatic point tracking was to use the initial manual points from the first slice and map these to all remaining slices in that series. The automatic point tracking system was written in C++ using the ITK 4.2 library (www.itk.org) (4) and requires two inputs: the list of initial points with physical co-ordinates (a CSV file output from the custom in-house software) and the corresponding initial DICOM image. Three main steps are performed:

1. The DICOM images for the initial image plane are identified and sorted by sequence number (tag 0020:0013). Centroids for organs were also calculated (if required).
2. The initial image is registered to each other image in the series. The method used was the 2D diffeomorphic demons (5) non rigid registration (ITK 4 implementation) with the following parameters: 4 level multi resolution pyramid (40,40,32,22 iterations); 256 histogram levels, 21 match points, threshold at mean intensity on, smooth deformation field turned on, standard deviations = 2.0, and smooth update field turned on.
3. The deformation field from step 2 was then used to map the list of initial points (and centroids) across to the corresponding target images. The mapped co-ordinates were also stored in a CSV file for analysis. The initial points were mapped to all other images (rather than the points from each image mapped to the next) to reduce error propagation throughout the series.

3. Results

3.1.1. Speed

Manual identification of points for all sagittal images (~235 images) for a single patient required between 120 to 240 minutes. The coronal images (~200 images) required an additional 120 to 180 minutes for an expert to contour. In comparison the automatic point propagation mapped all POIs from the initial image in ~230 seconds for all of the sagittal images (0.98s per slice) and ~269 seconds for all of the coronal images (1.35s per coronal slice).

3.1.2. Validation of automatic points

Validation results comparing automatic points versus manual points are summarised in Tables 1 and 2. Although validation was possible as manual points had been recorded for each image for each patient, the number of manual points varied on each image and points were recorded in an inconsistent order, therefore in the sagittal images centroids were compared for the bladder, prostate, seminal vesicles, rectum, and public symphysis; and the absolute position for the coccyx and skin marker. For the coronal images centroids were used for the bladder, prostate and seminal vesicles (absolute position was used for the femoral heads). The largest difference between manual and the automatic method occurred in the sagittal images, particularly for the rectum (AP), coccyx (AP) and bladder (SI). These differences generally appear to be registration errors from out of plane motion. Despite these challenges the difference between manual and automatic centroids was generally less than 1mm and were significantly correlated ($r>0.99$, $p<0.001$) for all organs in both the sagittal and coronal cine-MRI sequences.
Table 1. Mean difference ± standard deviation (mm) between manual and automatic sagittal centroid or landmark displacements (landmark points are marked with an asterisk). SV = Seminal Vesicles; Pubic S = Pubic Symphysis. Skin = skin marker.

|       | AP        | SI        |
|-------|-----------|-----------|
| Bladder | 0.68±2.41 | -1.64±2.57 |
| Prostate | 0.77±1.86 | 0.91±3.13  |
| SV     | 0.06±2.41 | -1.40±4.52 |
| Rectum | -2.40±4.46| -0.87±4.11 |
| Pubic S. | -0.02±1.43| 0.32±1.34  |
| Coccyx*| -1.76±7.57| 0.19±4.05  |
| Skin*  | -0.55±1.31| -1.66±3.51 |

Table 2. Mean difference ± standard deviation (mm) between manual and automatic coronal centroid or landmark displacements (landmark points are marked with an asterisk). SV = Seminal Vesicles; Pubic S = Pubic Symphysis.

|       | LR        | SI        |
|-------|-----------|-----------|
| Bladder | 1.42±3.22 | 0.27±2.28 |
| Prostate | -1.22±1.34| 1.85±4.13 |
| RT SV  | -0.66±1.42| -0.12±1.70|
| LT SV  | -0.04±1.69| 1.32±2.90 |
| RT Femur* | -0.15±1.39| -0.83±1.73|
| LT Femur*| -0.10±2.88| -0.87±1.66|

3.1.3. Automatic results
Automatic tracking results for all organ points were generated (based on the set of initial points) and are summarised in Tables 3 - 6. Patient 1 was found to have noticeably higher amounts of internal organ motion (particularly at the edges of the prostate and seminal vesicles).

Figure 2. Sagittal (left) and Coronal (right) accumulated deformation fields for study patient #2. The prostate, seminal vesicles and anterior part of the bladder show the most motion on the sagittal slice overlay (see also Table 3 and 4).
The results are either organ centroid or landmark displacements (landmark points are marked with an asterisk).

### Table 3. Mean ± standard deviation (mm) point tracking results (Sagittal AP direction) for each of the five study patients over all slices. SV = Seminal Vesicles; Pubic S = Pubic Symphysis; Skin = skin marker. The results are either organ centroid or landmark displacements (landmark points are marked with an asterisk).

| Patient ID | 1     | 2     | 3     | 4     | 5     |
|------------|-------|-------|-------|-------|-------|
| Bladder    | 3.88±2.67 | -0.15±1.53 | -0.71±1.66 | 1.74±2.01 | 1.42±2.14 |
| Prostate   | 7.17±2.41 | -1.49±1.01 | -1.35±1.10 | 2.11±1.96 | -1.19±1.11 |
| SV         | 5.60±2.01 | -2.02±1.08 | -1.66±1.23 | 3.14±1.97 | -0.80±1.40 |
| Rectum     | 3.48±2.46 | -1.41±0.94 | -1.01±1.82 | 0.86±2.37 | -1.48±0.67 |
| Pubic S.   | 4.81±2.13 | -0.51±0.52 | -0.71±1.19 | -0.12±0.57 | 0.02±0.55 |
| Coccyx*    | -2.45±2.43 | -0.59±0.41 | -0.83±0.62 | -0.12±0.13 | -0.90±0.39 |
| Skin*      | 2.63±1.05 | 0.28±0.30 | -1.66±0.77 | -0.18±0.98 | 0.11±0.84 |

### Table 4. Mean ± standard deviation (mm) point tracking results (Sagittal SI direction) for each of the five study patients over all slices. SV = Seminal Vesicles; Pubic S = Pubic Symphysis; Skin = skin marker. The results are either organ centroid or landmark displacements (landmark points are marked with an asterisk).

| Patient ID | 1     | 2     | 3     | 4     | 5     |
|------------|-------|-------|-------|-------|-------|
| Bladder    | 5.44±2.78 | -0.98±2.02 | -0.03±1.29 | 2.31±2.36 | 0.65±2.05 |
| Prostate   | 6.76±2.83 | -3.08±2.07 | -0.36±1.22 | -0.02±1.37 | -0.70±1.14 |
| SV         | 6.31±3.42 | -3.67±1.71 | 0.80±1.60 | 2.32±1.95 | 0.04±1.14 |
| Rectum     | 5.58±3.14 | -2.22±2.58 | 1.47±1.32 | 0.78±1.27 | 0.32±0.55 |
| Pubic S.   | 3.82±1.83 | -0.56±0.35 | -1.02±1.12 | -0.02±0.55 | -0.21±0.55 |
| Coccyx*    | 5.56±3.43 | -0.21±0.13 | 1.59±0.52 | -0.13±0.40 | -0.08±0.26 |
| Skin*      | 4.24±2.00 | -0.61±0.66 | -2.31±1.40 | -0.36±0.90 | -0.50±1.40 |

### Table 5. Mean ± standard deviation (mm) point tracking results (Coronal LR direction) for each of the five study patients over all slices. SV = Seminal Vesicles. The results are either organ centroid or landmark displacements (landmark points are marked with an asterisk).

| Patient ID | 1     | 2     | 3     | 4     | 5     |
|------------|-------|-------|-------|-------|-------|
| Bladder    | -0.86±2.39 | 1.06±3.37 | -1.73±2.93 | 0.27±2.20 | 0.48±2.07 |
| Prostate   | -1.01±2.30 | -1.83±2.12 | 0.29±1.52 | 0.78±1.36 | 0.24±1.64 |
| RT SV      | -1.63±2.06 | -1.07±1.28 | 0.92±1.70 | 1.14±1.73 | 0.26±0.88 |
| LT SV      | 0.61±1.65 | 0.27±0.93 | -0.72±1.10 | -0.25±1.14 | -0.79±1.01 |
| RT Femur*  | -1.13±1.06 | 0.36±0.15 | 0.67±1.11 | 0.08±0.07 | -0.29±0.13 |
| LT Femur*  | -0.93±0.56 | -0.32±0.20 | 0.31±0.78 | -0.39±0.10 | -0.51±0.23 |

### Table 6. Mean ± standard deviation (mm) point tracking results (Coronal SI direction) for each of the five study patients over all slices. SV = Seminal Vesicles. The results are either organ centroid or landmark displacements (landmark points are marked with an asterisk).

| Patient ID | 1     | 2     | 3     | 4     | 5     |
|------------|-------|-------|-------|-------|-------|
| Bladder    | 1.08±3.23 | -1.73±2.22 | 1.04±1.92 | 2.89±2.84 | 0.36±1.79 |
| Prostate   | 3.27±3.36 | -1.16±1.34 | -0.34±1.13 | 2.55±1.54 | 0.09±1.73 |
| RT SV      | 2.71±2.93 | -2.19±1.45 | 0.66±1.80 | 1.38±1.45 | 0.73±1.10 |
| LT SV      | 2.68±2.49 | -1.78±0.92 | 0.49±1.25 | 0.50±1.02 | -0.66±1.24 |
| RT Femur*  | -2.08±1.10 | -1.59±0.97 | 0.50±0.96 | 0.46±0.15 | 0.15±0.22 |
| LT Femur*  | -0.43±0.59 | -0.52±0.53 | 0.23±1.45 | 0.64±0.38 | -1.70±0.47 |
4. Discussion

The proposed system was in general an order of magnitude faster than manual point identification (reducing the time required from 4-7 hours per patient to 8 minutes). The automatic method enables fast quantification and visualization (Figure 2) of deformation during the cine-MRI acquisition time period. Another advantage of the method is that the motion of all voxels in the volume can be analysed, rather than just the user selected points. This could enable the discovery and quantification of areas of significant motion. One limitation of the current system is the requirement for manual points to be placed on the initial slice. Combining the tracking with an anatomical atlas (6) could be useful to initialise the set of points and to automatically analyse motion within all contoured structures within the atlas. As Tables 3-6 show, patient specific differences can be large (for example, patients 3 and 5 had much lower organ motion than patient 1). The method is easily adaptable to 3D cine-MRI by using 3D registration (7).

The system was validated successfully against manual points (generally <1mm difference) and was useful in detecting some input errors from the custom manual point recording software. A limitation of the proposed method when using 2D cine-MRI is unpredictable out of plane motion due to peristalsis, rectal gas and bladder related internal organ motion which led to some registration errors (this error occurs as image features being tracked can disappear from the target image). This difficulty could be overcome by verification from an expert observer or with 3D cine-MRI acquisition and registration.

Acknowledgments
Jason Dowling acknowledges funding support from the Cancer Council NSW (RG 11-05), Prostate Cancer Foundation of Australia (Y12011), Movember and Cure Cancer Australia. Cine MRI scans were funded by the CASS foundation.

References
1. Bayman NA, Wylie JP. When should the seminal vesicles be included in the target volume in prostate radiotherapy? Clinical oncology. 2007 Jun;19(5):302–7.
2. Chan P, Dinniwell R, Haider MA, Cho Y-B, Jaffray D, Lockwood G, et al. Inter- and intrafractional tumor and organ movement in patients with cervical cancer undergoing radiotherapy: a cinematic-MRI point-of-interest study. International journal of radiation oncology, biology, physics. 2008 Apr 1;70(5):1507–15.
3. Ghilezan MJ, Jaffray DA, Siewerdsen JH, Van Herk M, Shetty A, Sharpe MB, et al. Prostate gland motion assessed with cine-magnetic resonance imaging (cine-MRI). International journal of radiation oncology, biology, physics. 2005 Jun 1;62(2):406–17.
4. Ibanez L, Schroeder W. The ITK Software Guide 2.4. Kitware, Inc.; 2005.
5. Vercauteren T, Pennec X, Perchant A, Ayache N. Diffeomorphic demons: efficient non-parametric image registration. NeuroImage. 2009 Mar;45(1 Suppl):S61–72.
6. Dowling JA, Fripp J, Chandra S, Pluim JPW, Lambert J, Parker J, et al. Fast automatic multi-atlas segmentation of the prostate from 3D MR images. Prostate Cancer Imaging. Image Analysis and Image-Guided Interventions. Springer; 2011. p. 10–21.
7. Chandra S, Dowling J, Shen K, Raniga P, Pluim J, Greer P, et al. Patient Specific Prostate Segmentation in 3D Magnetic Resonance Images. IEEE Transactions on Medical Imaging. 2012 Aug 2;31.