A comparison of dose warping methods for 4D Monte Carlo dose calculations in lung

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Abstract. Dose calculation methods which incorporate tissue motion are an important tool for evaluating the effect of respiratory motion on the delivered dose distribution. 4D dose calculation methods use a sum of remapped doses calculated on 4D CT images of the patient at different respiratory phases to determine the cumulative dose received over the entire respiratory cycle. A number of methods for remapping the dose to the reference phase have been proposed, including center-of-mass (COM) tracking and trilinear (TL) interpolation. In this work we compare calculations of dose distributions remapped between extreme breathing phases against a 4D Monte Carlo dose code defDOSXYZ for three planning scenarios. No clinically significant differences were noted between dose distributions calculated by the three methods with the exception of an extreme motion evaluation case where TL and COM remapping underestimated the 95% target dose coverage by up to 16%. The accuracy of these dose calculation methods is significantly affected by the continuity of the deformation fields from non-linear image registration.

1. Introduction

Four dimensional (4D) dose calculation methods which incorporate organ motion and deformation are required to determine the effects of respiratory motion on the delivered dose distribution as well as to evaluate motion compensation techniques. A 4D dose calculation method employs voxel displacement maps obtained from non-linear image registration of 4D CT images to relate the dose calculated on different respiratory phases back to a reference (planning) phase. We term this process dose remapping. A number of dose remapping methods have been proposed which basically differ in terms of how the mapped dose is interpolated back to the reference dose grid. Previously we introduced an alternative method of 4D Monte Carlo dose calculation where the reference dose grid deforms according to the voxel displacement maps to reproduce anatomical deformations due to breathing. As the dose calculation grid is the same for calculation of dose at all breathing phases no interpolation is required. Furthermore, in our work we adjusted the density of the deformed voxels thus ensuring conservation of mass. Preliminary comparisons of dose calculations in a simple deforming phantom, where mass is conserved, between this defDOSXYZ code and a dose remapping method using trilinear interpolation indicated that the latter method underestimates the dose received in regions of steep dose gradients and large deformations. It was not clear, however, if these large discrepancies would occur in patient dose calculations.
In this study we compare three methods of 4D dose calculation using 4D CT images of lung patients and different planning scenarios.

2. Materials and Methods

2.1. Patient data
Two patients were included in this study. Patient 1 had a 5.2 cc tumour located in the upper left lobe which underwent a displacement of approximately 1.2 cm between exhale and inhale. Patient 2 had a 112 cc primary target volume located in the right lower lobe with mediastinal nodal involvements of 63 cc and 12 cc, respectively. The primary target volume underwent a maximum breathing excursion of 9 mm.

Thoracic 4D CT images for Patient 1 were acquired at the MD Anderson Cancer Centre using the axial mode of a Discovery ST PET-CT scanner (GE Medical Systems, Milwaukee, WI). Scans were retrospectively sorted into ten breathing phases with an image resolution of 0.98 mm and slice thickness of 2.5 mm. Images for Patient 2 were similarly acquired at the Massachusetts General Hospital using a Lightspeed Qx/I 4-slice CT scanner (GE Medical Systems, Milwaukee, WI).

2.2. Non-linear image registration
Non-linear image registration was performed between the extreme breathing phases. For Patient 1 the reference phase was Inhale and the target phase was Exhale. Registration was performed using the ANIMAL non-linear image registration algorithm using a multiresolution registration process ending with a deformation lattice spacing equal to the image resolution. For Patient 2, registration between the exhale and inhale phase was performed using a B-splines method.

2.3. Treatment plans
Three different treatment planning scenarios were considered. Patient 1 was planned using a 2-field 18 MV 3D-CRT plan with the CADplan (Varian Medical Systems, Palo Alto, CA) treatment planning software. The target was delineated on the reference inhale phase and a 7 mm margin was added for microscopic extent. Two planning strategies were considered for this patient, termed “tracking” (1) and “motion evaluation” (2). For the tracking case a treatment plan was defined on the target exhale phase and in the latter case the plan was defined on the inhale phase, in both cases the dose received at exhale remapped to the inhale phase was evaluated. The prescription dose in both cases was 60 Gy.

Patient 2 was planned using a 5-field IMRT plan with the CORVUS treatment planning software (NOMOS, Cranberry Township, PA). Internal target volume margins were determined based on a fusion of target volumes drawn on separate phases of the 4D CT image set and a further 8 mm expansion was added for the planning target volume. The prescribed dose was 63 Gy.

2.4. Dose calculations

2.4.1. Monte Carlo simulations
Phase space files were generated using BEAMnrc/EGSnrcMP. For Patient 2 transport through the jaws and MLC was performed using the model developed by Siebers et. al. modified for multiple Compton scatter.

Two separate patient dose calculations were performed. For the dose calculations employing dose remapping the DOSXYZ/EGSnrcMP Monte Carlo code was used to calculate the dose distribution on a patient density matrix generated from the transformed reference anatomy. We use the transformed anatomy instead of the target phase anatomy to eliminate errors introduced by registration inaccuracies. The second dose calculation was performed using the defDOSXYZ/EGSnrcMP code. Both sets of calculations used the same phase space file, transport parameters and number of histories. ECUT and PCUT were set to 0.7 MeV and 0.001 MeV, respectively and the EXACT boundary crossing algorithm with a skin depth of 3 electron mean free paths was used.
2.4.2. Dose warping methods

Three methods of 4D dose calculation were compared: warping dose distributions calculated with DOSXYZ using COM remapping, using Trilinear remapping with octant subdivision and dose calculations using the deformable voxel tracking code defDOSXYZ.

For the first two methods the dose calculated on the transformed reference anatomy was remapped to the reference phase using the deformation vectors interpolated at the center of mass (COM) of each voxel. For each reference voxel the COM is mapped to its corresponding location on the transformed anatomy using these vectors. For the COM tracking method the dose to this reference voxel is given by the dose, in the transformed anatomy dose distribution, in the voxel which overlaps the remapped COM. For the trilinear remapping method the reference voxels are first subdivided into octants, then the COM of each octant is remapped to the transformed anatomy and the dose at each remapped COM is interpolated from the dose distribution calculated on the transformed anatomy. The dose in each reference voxel is the average of the remapped dose for each octant.

For the defDOSXYZ calculations the same deformation vectors are used to deform the reference dose grid to match the transformed anatomy and the dose distribution is calculated on this deformed geometry. As the same dose grid is retained, the dose at the reference state may be directly determined from the dose received in the deformed voxels.

The remapped dose distributions calculated by the three methods were compared in terms of dose difference maps, mean dose ($D_{\text{mean}}$) and dose-volume histograms (DVHs).

3. Results and Discussion

3.1. Non-linear image registration

Based on expert-identified homologous points the average accuracy of deformable registration in the lungs was evaluated to be 1.2 ± 1.2 mm for Patient 1 and 4.2 ± 2.4 mm for Patient 2.

3.2. Patient 1: tracking scenario

Inhale-to-Exhale DVHs for the CTV as determined by the 3 dose calculation methods are shown in Figure 1(a). The dose grid resolution is 4x4x2.5 mm$^3$. The average statistical uncertainty on the dose in the CTV is within 2%.

![Figure 1](https://example.com/fig1)

(a)  (b)

Figure 1. CTV dose volume histograms of dose remapped from Exhale to Inhale for Patient 1 tracking scenario for a dose grid resolution of 4x4x2.5 mm$^3$.

Though at first it appears to be not statistically significant, there is a systematic 2-3% offset in dose between defDOSXYZ and remapping calculations. Comparison of the deformed reference voxel densities, on which defDOSXYZ calculations are performed, and the voxel densities in the transformed reference image, on which DOSXYZ calculations are performed for dose remapping.
revealed an average 2% difference in density between these images. The deformation vectors obtained from the ANIMAL image registration software are obtained from a registration process that does not have mass conservation as a constraint. This causes the lung density to be higher in the deformed inhale images compared to the transformed inhale images. We therefore decided to repeat the defDOSXYZ calculations without adjusting the voxel densities as they were deformed (see Figure 1(b)). In this case the mass of the deformed voxel image was verified to be equal to the mass of transformed image. The removal of the mass conservation from defDOSXYZ calculations resulted in a 1% decrease in the mean dose and improved the agreement with the dose remapping calculations. To make comparisons fair, for all subsequent studies we used these non-density adjusted dose calculations.

The dose distributions for the three methods are shown in Figures 2 (a) through (c). Two main observations can be made. First, the isodose lines extend more inferiorly into the lung for the defDOSXYZ calculation compared to remapping methods, which can be attributed to the limitations of interpolation methods in regions where dose gradients exist. The second observation is that there exist localized regions of discrepancy at tissue interfaces, for example at the right edge of the tumour and the chest wall/lung interfaces (indicated by arrows). The dose deformations in these regions are not correctly predicted by the remapping methods because the dose distribution is calculated on the transformed image which has to be resampled to a rectangular grid. Partial volume averaging of voxel intensities leads to inconsistencies in the patient representation in such regions of sharp density gradients. In the case of the tumour/lung interface, this contributes to the reduced shoulder of the CTV DVH for the remapping methods compared to defDOSXYZ.

![Figure 2. Dose distributions for Patient 1 tracking case on reference (inhale) phase. Dose distributions are normalized to the prescription dose of 60 Gy.](image)

A 0.6% difference in the mean dose between the trilinear and COM remapping methods was noted. Essentially the DVH for the COM remapping calculation appears to be a lower resolution version of the TL remapping calculation. This result is intuitive since the TL remapping uses octant subdivision the resolution of this method is inherently higher compared to COM remapping. The dose distributions
for the remapping methods are similar, although in the case of TL remapping the dose distribution is smoother because interpolation of the remapped dose is performed.

To determine the factors which lead to differences between the remapping and defDOSXYZ calculations we calculated the normalized cross-correlation between the local dose differences and deformation magnitude, fractional volume change and dose gradient. The correlation values were calculated over the whole dose grid (128x128x80). For TL remapping discrepancies were most strongly correlated with the local dose gradient. For COM remapping dose discrepancies were more strongly correlated with deformation vector magnitude. For COM remapping it can be expected that as the deformation magnitude increases deformed voxels are increasingly less aligned with the rectangular voxels of the dose distribution to be remapped. In this case, due to lack of interpolation, simple point dose remapping does not accurately estimate the remapped dose.

3.3. Case 2: Patient 1 motion evaluation scenario

Inhale-to-Exhale dose volume histograms for the CTV determined by the 3 dose calculation methods are shown in Figure 3 for two different dose grid resolutions. In this case the plan was not designed to cover the tumour in the target phase so there are significant dose gradients across the CTV which manifests as a reduced shoulder of the DVH (D95%) compared to the tracking scenario. In this case defDOSXYZ calculations predict a 13% and 16% reduction in the D95% compared to COM and TL remapping, respectively. Reducing the voxel size somewhat improved the agreement between the three calculations, most notably between the remapping methods, but did not resolve the discrepancies between defDOSXYZ calculations and dose remapping. When the total accumulated dose over the whole breathing cycle is considered the discrepancies are reduced to 4% and 5% for COM and TL remapping, respectively.

3.4. Case 3: Patient 2 ITV plan

Exhale-to-Inhale dose volume histograms for the three target ITVs determined by the 3 dose calculation methods are shown in Figure 4 for a dose grid resolution of 4x4x5 mm3. The DVH for dose delivery at the exhale phase was included to illustrate the effect of motion. The average statistical uncertainty on the dose calculation in the target volumes was approximately 5%. The removal of the voxel density adjustment in defDOSXYZ calculations resulted in a 2% decrease in mean dose and improved agreement with remapping methods. However there was still a greater than 5% discrepancy in the D95%, minimum and maximum doses calculated by these methods.

This continued systematic offset of defDOSXYZ calculations was attributed to sharp gradients in the deformation vectors. This hypothesis was tested by repeating the dose calculations for one field using deformation vectors smoothed with a Gaussian kernel of FWHM 32,32,40 mm. When the
deformation vectors are smoothed there are no differences between the defDOSXYZ, remap TL and remap COM calculations. The defDOSXYZ DVH was unchanged by vector smoothing compared to the remapping methods. This indicates that the dose distributions calculated by dose remapping methods are influenced by not only the magnitude but also the pattern and gradients in the deformation vectors.

![Graphs](image1.png)

(a) ITV1
(b) Heart

Figure 4. DVHs for primary target volume and Heart for Patient 2 ITV plan scenario.

![Graphs](image2.png)

(a) Jacobian map of fractional volume change
(b) Z component of deformation magnitude

Figure 5. Axial images of (a) fractional volume change and (b) Z component of deformation magnitude. Target volume and heart contours are shown in black.

4. Conclusion

For realistic treatment planning scenarios no clinically significant differences were noted between dose remapping and defDOSXYZ calculations. However, for an extreme case where target motion was not included in the plan, the target volume coverage was underestimated by up to 16% by remapping methods. Definitive conclusions about the discrepancies between dose calculation methods requires further investigation with a larger patient set. Dose discrepancies between defDOSXYZ and remapping methods were found to correlate most strongly with the gradient of the dose distribution. The validity of the comparison between the dose calculation methods was affected by inconsistent handling of mass conservation between image registration and dose calculation with defDOSXYZ. The accuracy of all the dose remapping methods was influenced by the continuity of deformation vector fields as determined by non-linear image registration. It is essential that a physically realistic, continuous, deformation field is used for these dose calculations.
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