

Purpose: To develop a comprehensive high accuracy procedure for computing respiratory motion from 4D-CT image datasets. The estimated motion field is applied to model and predict respiratory behavior at different breathing states. **Method and Materials:** The 4D-CT image data consisted of 16-slice CT volume segments acquired in cine mode. We used the optical flow deformable image registration algorithm to register the image segments to a common reference 3D-CT volume. Before registration, the segments were optimally aligned to the reference volume according to the measured tidal volumes and the positions of the diaphragm apex in the inhaled and exhaled phases. Image registration was applied using a multiresolution approach and a feature-preserving image down-sampling filter, the max filter, to achieve faster computation speed and better registration accuracy. Computed backward motion fields were inverted to obtain the forward motion fields. Registration accuracy was validated using anatomical landmarks and a digital phantom. The motion fields were fit using 5D (spatial 3D + tidal volume + air flow rate) motion models independently applied to the forward and inverse motion vector maps. The forward model characterized how the tissue moved, and the inverse model characterized how the CT image density changed with respect to the tidal volume and the air flow rate. Target modeling errors (TME), modeling errors (ME) and modeling prediction errors (MPE) were computed to evaluate these 5D models. **Results:** The registration error was less than 1.1 ± 0.8 mm for lung tissue. For the forward model, TME = 0.6 ± 0.4 mm, ME and MPE were both 0.3 ± 0.5 mm. For the inverse model, TME = 1.1 ± 0.6 mm, ME = 0.5 ± 0.4 mm and MPE = 0.4 ± 0.5 mm. **Conclusion:** Our procedure computes 4D respiration motion with high accuracy. Both 5D models could be utilized in multiple radiation oncology applications, including tumor motion tracking and 4D treatment planning.