

Purpose: To develop a novel method for registration of different phases of 4D CT with consideration of lung volume deformation and sliding motion. **Method and Materials:** Sliding motion of the lung against chest wall during breathing presents a challenging problem in image registration. The motion range of diaphragm during respiration is about 3 cm and the displacement vectors of tissue on the two sides of pleura are discontinuous. To register different phases of 4D CT, the lungs on these phases were first automatically segmented. A Scale Invariance Feature Transformation (SIFT) descriptor was used to find feature points shared by the template phase and target phases on the lung contours. A Fourier transformation of displacements of featured points was carried out. The low spatial frequency component of the displacement represents the sliding motion, whereas the high frequency component of the Fourier transformation represents the contribution from deformation and can be modeled by a conventional deformable model. After shifting the lungs on the target phase according to the filtered sliding displacements, a thin plate spline (TPS) deformable registration was applied between the template phase and shifted phases to obtain the displacement vector for each voxel. **Results:** We calculated the average diaphragm sliding distance between phase 1 and other phases with and without inclusion of lung sliding using patient data. It is demonstrated that the accuracy of the proposed method is three times better than that of conventional TPS method. With inclusion of sliding motion, the overlapped ratio of tumor contour is increased to 84.3% as compared to 78.0% using conventional approach. **Conclusions:** A hybrid method of deformable registration in spatial domain and low-pass filter in frequency domain seems to model the lung breathing motion well. The combination provides a robust and computationally efficient method for registration of 4D CT thoracic images.