Radiation therapy has been successful in treating lung cancer patients, but its efficacy is limited by the inability to account for the respiratory motion during treatment planning and radiation dose delivery. Physically based lung deformation models facilitate the computation of both tumor motion and motion of local lung tissue during radiation therapy. In this dissertation, a novel method is discussed to accurately register the 3D lungs obtained from 4D-CT at one respiratory phase to another, which facilitates the estimation of the volumetric lung deformation models. A multi-level and multi-resolution optical flow method coupled with thin plate splines (TPS) based registration is proposed, which enables higher accuracy in regions with inconsistent intensity, as compared to multi-resolution optical flow and other registration methods. Validation results with clinical experts show that the lung registration is computed within 2-voxel distance Root Mean Square (RMS) error.