Uncertainties in the precise locations of tumor voxels are inherent for a variety of reasons. It is therefore desirable to take those uncertainties into account, and further, to derive treatment planning methodologies that directly utilize information (e.g. probability distributions or actual trajectories) about the location of the target, including spatial uncertainties, so that resulting treatment plans exhibit normal tissue dose reduction, and potentially higher tumor doses.

Two novel robust approaches are investigated. 1) Under-dose probability (UDP) estimates the probability of the tumor receiving a dose less than a user-defined critical dose. It can be modeled using linear mixed-integer programming techniques. 2) Probability dose generation (PDG) designs treatment plans in which the probability of a voxel located in a target is factored during the dose generation process. Utilizing 4D-CT scans of lung/liver cancer patients during different breathing phases (phases 0-9, 0:full-inhale, 5:full-exhale), four treatment planning strategies are compared. 1) Standard planning with a static PTV based on a single selected phase (control). 2) The Internal Target Volume (ITV) approach, where ITV is defined as the union of CTVs in all breathing phases. 3) Plans obtained with UDP. 4) Plans obtained via PDG. Sophisticated computational optimization techniques are used to solve each of these models.

Compared to Standard and ITV plans, UDP and PDG plans offer good coverage, comparable minimum PTV-dose, improved PTV-conformity, and higher PTV-dose. In addition, in lung, PDG reduces normal-lung-mean-dose by 13% and heart-mean-dose by 20%; and UDP reduces esophagus-mean-dose by 70% and heart-mean-dose by 49%. In liver, PDG reduces normal-liver-mean-dose by 8% and other-normal-tissue-mean-dose by 26%, whereas UDP reduces normal-liver-mean-dose by 10%, both with improved PTV-conformity of 7%.

Thus, the UDP and PDG approaches can result in treatment plans of increased robustness, they allow a reduction in mean dose to organs-at-risk and normal tissue, and in some cases, deliver higher dose to the tumor volume.