Previously, we described a method to incorporate the effects of patient setup uncertainties and organ motion due to breathing into 3-D dose calculations for conformal therapy of liver disease. This method is based on a convolution of the static 3-D dose grid with distribution functions representing the setup uncertainties in three dimensions and a mathematical function describing the motion of the liver due to breathing. We showed the convolution-based methods to be sufficient in predicting the mean expected dose distribution, D, in the face of these uncertainties through comparison to Monte Carlo-based direct simulation. However, because patients receive treatment using a finite number of fractions, the actual dose distribution realized by each patient will generally differ from the mean expected dose distribution. Direct simulation methods can predict the range of expected outcomes, but such approaches can be quite inefficient. Therefore, we have generalized our original method to allow for an efficient calculation of both the dose D and the variance in D, σ^2_D, at any point within that 3-D dose distribution. Our methodology is presented, together with examples of the implementation of these more realistic dose calculations in (i) the interpretation of target volume coverage in conformal therapy trials, and (ii) conformal therapy dose escalation studies based on estimation of the distribution of dose to a critical organ.

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