Purpose: To build a biophysical risk model of radiation pneumonitis (RP) using a Bayesian Network (BN) framework for combining biomarker information with dosimetric parameters.

Methods: 22 non-small-cell lung cancer patients who received radiotherapy (RT) between 2006 to 2009 were selected. Blood samples were collected from each patient before and during RT. From each sample the concentration of the following four candidate biomarkers were measured: alpha-2-macroglobulin (a2M), angiotensin converting enzyme (ACE), transforming growth factor β (TGF-β), and interleukin-6 (IL-6). The biomarker information was reduced to a subset of variables whose linear combination showed the highest correlation with RP via logistic regression analysis. The selected biomarker variables were combined with two dosimetric known RP parameters (mean lung dose, tumor position in superior-inferior direction) as features to learn a BN classifier for predicting RP onset. Predictive power of the learned BN classifier was compared with a logistic regression and Naïve Bayes classifiers in a simulated validation dataset.

Results: The following 5 biomarker variables were selected for BN learning: 1) pre-RT concentration level of a2M, 2) ratio of pre- to intra-RT levels of a2M, 3) intra-RT IL-6 level, 4) ratio of pre- to intra-RT levels of TGF-β, and 5) pre-RT ACE level. The learned BN structure identified the probabilistic relations amongst the 7 features and RP where the role of a2M as a mediator of biological interaction was noticed. Performance of the BN classifier was 0.873, 0.959, and 0.676 for overall classification accuracy, positive and negative predictive power, respectively. It outperformed a logistic regression and a Naïve Bayes counterpart in terms of overall accuracy and positive predictive value.

Conclusions: The presented BN approach has a potential to enhance the prediction power of RP by explicitly modeling interactions between physical and biological variables, which can also be used to validate or guide further biomarker research of RP.