Prediction of lung cancer using volatile biomarkers in breath

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Abstract: **Background:** In patients with lung cancer, induction of high risk cytochrome p450 genotypes may also accelerate catabolism of volatile organic compounds (VOCs) produced by normal metabolism (e.g. alkanes and alkane derivatives). A breath test for these VOCs can detect alterations in their abundance, and potentially identify a set of biomarkers of lung cancer. **Methods:** VOCs in 1.0 L alveolar breath collected over 2.0 min were analyzed in 195 patients with untreated primary lung cancer and 212 control subjects without lesions at chest CT. 268 subjects were randomly assigned to a training set to construct a fuzzy logic model of breath VOC markers of lung cancer, and 139 to a prediction set, where the model was tested as a predictor of lung cancer. **Results:** A fuzzy logic model employing 29 VOCs predicted primary lung cancer with 90.6% sensitivity, 82.7% specificity, and 0.91 area under curve (AUC) of the receiver operating characteristic (ROC). When all 407 subjects were combined in a leave-one-out analysis employing 29 VOCs, the model predicted primary lung cancer with 81.5% sensitivity, 87.3% specificity, 0.91 AUC, negative predictive value=99.6% and positive predictive value=11.6%. ROC curves were similar in TNM stages 1 through 4. The breath test predicted lung cancer in post-operative primary lung cancer patients (77/80), and in pre-operative and post-operative cases of cancer metastatic to lung from another site (12/13), mesothelioma (6/6), and suspicious chest imaging without biopsy evidence of cancer (40/41). **Conclusions:** Lung cancer, including early stage, can be predicted with a two-minute breath test for VOCs.