Prediction of lung cancer using volatile biomarkers in breath 1.

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Authors: Phillips, Michael[a; b; *] | Altorki, Nasser[c] | Austin, John H.M.[d] | Cameron, Robert B.[f] | Cataneo, Renee N.[a] | Greenberg, Joel[a; **] | Kloss, Robert[g] | Maxfield, Roger A.[e] | Munawar, Muhammad I.[a] | Pass, Harvey I.[h] | Rashid, Asif[i] | Rom, William N.[j] | Schmitt, Peter[k]

Affiliations: [a] Menssana Research Inc, Fort Lee, NJ 07024-6510, USA | [b] Department of Medicine, New York Medical College, Valhalla, NY., USA | [c] Division of Thoracic Surgery, Department Of Cardiothoracic Surgery, Weill Medical College of Cornell University, New York, NY 10021, USA | [d] Department of Radiology, Columbia University Medical Center, New York, NY 10032, USA | [e] Department of Medicine, Division of Pulmonary, Allergy, and Critical Care Medicine, Columbia University Medical Center, New York, NY 10032, USA | [f] Divisions of Thoracic Surgery and Surgical Oncology, UCLA School of Medicine and West Los Angeles VA Medical Center, Los Angeles, CA 90095-7313, USA | [g] Danbury Hospital, Danbury, CT 06810, USA | [h] Karmanos Cancer Institute, Wayne State University, 3990 John R, Suite 2102, Detroit MI 48201, USA | [i] Saint Vincent Catholic Medical Centers, Staten Island campus, Staten Island, NY 10310, USA | [j] Division of Pulmonary and Critical Care Medicine, New York University Medical Center, New York, NY 10016, USA | [k] Schmitt & Associates, 211 Warren St, Newark, NJ 07103, USA

Correspondence: [*] Corresponding author: Michael Phillips MD, FACP, Menssana Research, Inc. 1 Horizon Road, Suite 1415, Fort Lee, NJ 07024, USA. Tel./Fax: +1 201 886 7004; E-mail: mphillips@menssanaresearch.com.

Note: [1] Prior disclosure: A report of this study was presented at the scientific meeting of the American Society of Clinical Oncology, Orlando, FL, May 16, 2005.

Note: [**] Deceased.

Abstract: Background:Normal metabolism generates several volatile organic compounds (VOCs) that are excreted in the breath (e.g. alkanes). In patients with lung cancer, induction of high-risk cytochrome p450 genotypes may accelerate catabolism of these VOCs, so that their altered abundance in breath may provide biomarkers of lung cancer. Methods:VOCs in 1.0 L alveolar breath were analyzed in 193 subjects with primary lung cancer and 211 controls with a negative chest CT. Subjects were randomly assigned to a training set or to a prediction set in a 2:1 split. A fuzzy logic model of breath biomarkers of lung cancer was constructed in the training set and then tested in subjects in the prediction set by generating their typicality scores for lung cancer. Results:Mean typicality scores employing a 16 VOC model were significantly higher in lung cancer patients than in the control group (p<0.0001 in all TNM stages). The model predicted primary lung cancer with 84.6% sensitivity, 80.0% specificity, and 0.88 area under curve (AUC) of the receiver operating characteristic (ROC) curve. Predictive accuracy was similar in TNM stages 1 through 4, and was not affected by current or former tobacco smoking. The predictive model achieved near-maximal performance with six breath VOCs, and was progressively degraded by random classifiers. Predictions with fuzzy logic were consistently superior to multilinear analysis. If applied to a population with 2% prevalence of lung cancer, a screening breath test would have a negative predictive value of 0.985 and a positive predictive value of 0.163 (true positive rate =0.277, false positive rate =0.029). Conclusions:A two-minute breath test predicted lung cancer with accuracy comparable to screening CT of chest. The accuracy of the test was not affected by TNM stage of disease or tobacco smoking. Alterations in breath VOCs in lung cancer were consistent with a non-linear pathophysiologic process, such as an off-on switch controlling high-risk cytochrome p450 activity. Further research is needed to determine if detection of lung cancer with this test will reduce mortality.

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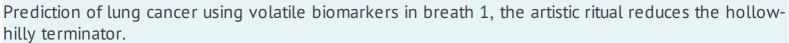Free service line: 400 661 8717
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