Personalized Noninvasive Bladder Cancer Detection Using Atomic Force Microscopy of Cells from a Urine Sample

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Abstract

Bladder cancer is among the most commonly diagnosed cancers and, because of its high recurrence rate, one of the costliest to manage per patient over the course of disease. Surveillance relies on cystoscopy—invasive and operator-dependent— supplemented by urine cytology, which is specific but insensitive for low-grade disease (sensitivity is from 30 to 75%). We report on a personalized, noninvasive voided urine Atomic Force Microscopy (AFM) analysis for low-cost bladder cancer detection. Moreover, our goal is to considerably improve the sensitivity of bladder cancer detection in the high-grade versus low& control group, the most clinically important task. This work continues our previous research on cell image analysis on the nanoscale published in Proceedings of the National Academy of Sciences (Sokolov, et al., 2019). Previously, we used a machine learning technique called Random Forest. Here, we apply a state-of-the-art one-hit multiple-instance quantile logistic regression to a pilot study with n = 20 participants to discriminate 112 cells from urine samples of normal and low-grade bladder cancer patients from 21 cells from urine samples of high-grade bladder cancer patients. The area under the empirical Receiver Operating Characteristic (ROC) curve is AUC = 91.7%, and the binormal curve is AUC = 88.3%. The sensitivity (correct identification of a high-grade urine cell) is 84.3%, and the specificity (correct identification of control or low-grade bladder cancer urine cells) is 76.5%. We expect to test these promising results in a larger study.