SELDI-TOF MS Whole Serum Proteomic Profiling with IMAC Surface Does Not Reliably Detect Prostate Cancer

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BACKGROUND: The analysis of bodily fluids using SELDI-TOF MS has been reported to identify signatures of spectral peaks that can be used to differentiate patients with a specific disease from normal or control patients. This report is the 2nd of 2 companion articles describing a validation study of a SELDI-TOF MS approach with IMAC surface sample processing to identify prostatic adenocarcinoma.

METHODS: We sought to derive a decision algorithm for classification of prostate cancer from SELDI-TOF MS spectral data from a new retrospective sample cohort of 400 specimens. This new cohort was selected to minimize possible confounders identified in the previous study described in the companion paper.

RESULTS: The resulting new classifier failed to separate patients with prostate cancer from biopsy-negative controls; nor did it separate patients with prostate cancer with Gleason scores <7 from those with Gleason scores ≥7.

CONCLUSIONS: In this, the 2nd stage of our planned validation process, the SELDI-TOF MS–based protein expression profiling approach did not perform well enough to advance to the 3rd (prospective study) stage. We conclude that the results from our previous studies—in which differentiation between prostate cancer and noncancer was demonstrated—are not generalizable. Earlier study samples likely had biases in sample selection that upon removal, as in the present study, resulted in inability of the technique to discriminate cancer from noncancer cases.

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Each year prostatic adenocarcinoma is diagnosed in almost 220,000 men and is responsible for about 27,000 deaths, making it the 2nd leading cause of cancer death in men in the US (1). Because prostate cancer diagnosed while still localized to the prostate can be cured by a number of local therapies, early detection of this disease is a commonly practiced clinical strategy.

Screening for increased concentrations of prostate-specific antigen (PSA)10 in serum is currently the most valuable approach for early detection of prostate cancer. Several large studies have reported that PSA alone is superior to digital rectal examination (DRE) and that PSA combined with DRE is the most effective early detection approach for prostate cancer (2–6). Widespread PSA screening programs have been associated with significant reduction in tumor stage at diagnosis and decreased numbers of cases diagnosed with metastases or poorly differentiated disease (7–9). Although the positive predictive value (PPV) of PSA has been reported as >80% for men with PSA concentrations >20 μg/L, the PPV may be as low as 15% in men with serum PSA concentrations <4 μg/L. Unfortunately, if diagnosed when PSA concentrations exceed 10 μg/L, many men will have advanced disease (5, 7). Because PSA is prostate specific rather than prostate cancer specific, increased concentrations of PSA are found in benign prostatic hyperplasia (BPH) (10),

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Received May 7, 2007; accepted October 17, 2007.
Previously published online at DOI: 10.1373/clinchem.2007.091496

10 Nonstandard abbreviations: PSA, prostate-specific antigen; DRE, digital rectal examination; PPV, positive predictive value; EDRN, Early Detection Research Network; DMCC, EDRN Data Management and Coordinating Center; EVMS, Eastern Virginia Medical School; Dx, diagnostic; UAB, University of Alabama; AUC, area under the curve; NPV, negative predictive value.