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Ultra-Sensitive Point-Of-Care Detection of PSA Using an Enzyme- and Equipment-Free Microfluidic Platform

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Abstract : Prostate cancer is one of the leading causes of cancer-related death among men. Prostate-specific antigen (PSA), a specific product of prostatic epithelial cells, is an important indicator of prostate cancer. Though PSA is not a specific serum biomarker for the screening of prostate cancer, it is recognized as an indicator for prostate cancer recurrence and response to therapy for patient's post-prostatectomy. Since radical prostatectomy eliminates the source of PSA production, serum PSA levels fall below 50 pg/mL, and may be below the detection limit of clinical immunoassays (current clinical immunoassay lower limit of detection is around 10 pg/mL). Many clinical studies have shown that intervention at low PSA levels was able to improve patient outcomes significantly. Therefore, ultra-sensitive and precise assays that can accurately quantify extremely low levels of PSA (below 1-10 pg/mL) will facilitate the assessment of patients for the possibility of early adjuvant or salvage treatment. Currently, the commercially available ultra-sensitive ELISA kit (not used clinically) can only reach a detection limit of 3-10 pg/mL. Other platforms developed by different research groups could achieve a detection limit as low as 0.33 pg/mL, but they relied on sophisticated instruments to get the final readout. Herein we report a microfluidic platform for point-of-care (POC) detection of PSA with a detection limit of 0.5 pg/mL and without the assistance of any equipment. This platform is based on a previously reported volumetric-bar-chart chip (V-Chip), which applies platinum nanoparticles (PtNPs) as the ELISA probe to convert the biomarker concentration to the volume of oxygen gas that further pushes the red ink to form a visualized bar-chart. The length of each bar is used to quantify the biomarker concentration of each sample. We devised a long reading channel V-Chip (LV-Chip) in this work to achieve a wide detection window. In addition, LV-Chip employed a unique enzyme-free ELISA probe that enriched PtNPs significantly and owned 500-fold enhanced catalytic ability over that of previous V-Chip, resulting in a significantly improved detection limit. LV-Chip is able to complete a PSA assay for five samples in 20 min. The device was applied to detect PSA in 50 patient serum samples, and the on-chip results demonstrated good correlation with conventional immunoassay. In addition, the PSA levels in finger-prick whole blood samples from healthy volunteers were successfully measured on the device. This completely stand-alone LV-Chip platform enables convenient POC testing for patient follow-up in the physician's office and is also useful in resource-constrained settings.

Keywords : point-of-care detection, microfluidics, PSA, ultra-sensitive
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