

# The detection of prostate cancer in urine samples after DRE, by CellDetect® – a novel staining method

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## Background

Elevated serum PSA often triggers prostate biopsies. However, PSA is not sensitive neither specific, and as a result prostate cancer (PC) may be missed when relying on a low PSA level to defer from biopsy, and unnecessary biopsies are often done when the PSA is elevated but cancer is not detected. With PSA levels between 4.0-10.0ng/ml, the sensitivity and specificity for cancer are 20-30% and 80-90%, respectively. We sought to explore prostate cancer detection by CellDetect® staining of prostate cells expelled into the urine following standardized digital rectal examination.

CellDetect® staining is a cytochemical stain derived from a plant extract aimed to add color differentiation to cytomorphological examination. This stain has been shown to depict benign cells in a green color as opposed to cancer which stains red. This effect has been consistent in various malignancies including bladder and cervical cancer.

## Purpose

The aim of the study was to determine the sensitivity, specificity and overall accuracy of CellDetect® in diagnosing PC in urine samples following digital rectal examination (DRE).

## Method

Our study included a research group of newly diagnosed PC patients that was compared with a control group with either a serum PSA level <2.5ng/ml or a recent negative prostate biopsy. All patients and controls underwent standardized DRE according to PCA3 test specifications (figure 1). Following the DRE, voided urine samples were collected, fixed and processed.

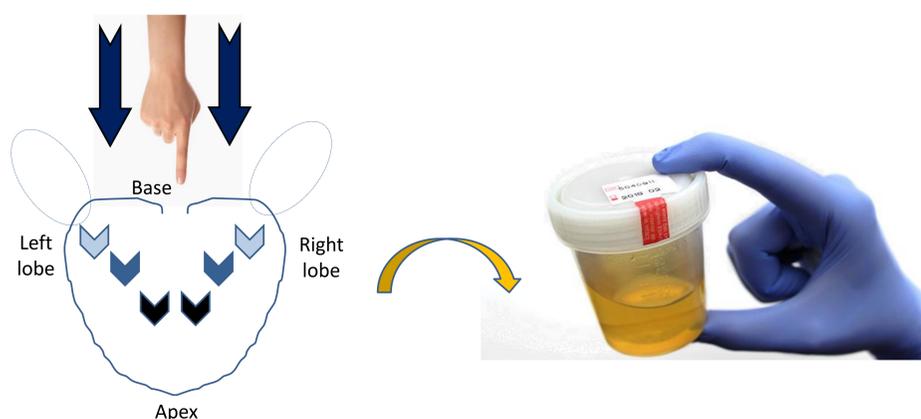


Figure 1: illustration of DRE procedure and urine collection.

CellDetect® staining was performed and results were inspected by a pathologist (AS). Samples were defined positive when cytomorphological atypical epithelial cells consistent with prostatic origin and violet-red nuclei were present. A sample was considered negative if cytology appeared benign and nuclei were stained green/purple or light pink. Any discordance between staining and pathology defined the samples as undetermined. CellDetect® performance evaluation (sensitivity, specificity, positive and negative predictive values and overall accuracy) was calculated.

## Patients Characteristics

Prostate cancer patients	Average /No.	Range or %	Control patients	Average /No.	Range or %
Age (years)	69	52-90	Age (years)	68	59-83
Pre biopsy PSA (ng/ml)	24	1.7-506	Serum PSA (ng/ml)	3.54	0.2-13.9
<b>Gleason score</b>			<b>Negative biopsy</b>	11	55%
3+3	18	53%			
3+4; 4+3	7	20%			
≥8	9	27%			
<b>T stage</b>					
T1	15	44%			
T2	15	44%			
T3-4	4	12%			
<b>Metastasis</b>	3	9%			
Prostate volume (ml)	61	20-300			
No. cores involved (median)	4	1-13			

Table 1: Patients characteristics enrolled into the study divided to control and cancer cases.

## Results

A total of 78 urine samples were included; 40 PC patients and 38 controls. Of those, 61 received determined diagnoses (78%).

Diagnostic accuracy was calculated on 34 PC samples and 27 control samples. Diagnoses analysis are summarized in table 2.

	CellDetect® positive	CellDetect® negative	Total
<b>Prostate cancer patients</b>	30 (TP)	4 (FN)	34
<b>Control patients</b>	7 (FP)	20 (TN)	27
<b>Total</b>	37	24	61

Table 2: Results deviation according CellDetect® readings. abbreviation: TP – true positive, FN – false negative, FP – false positive, TN – true negative

Our results showed that the CellDetect test for prostate cancer had a sensitivity of **88%**, **74% specificity**, **81% positive predictive value**, **83% negative predictive value** and an **overall accuracy of 82%**.

Of 7 FP patients, 4 underwent a repeated 14 core prostate biopsy which was negative, One patient declined a biopsy and in 2 others results are pending

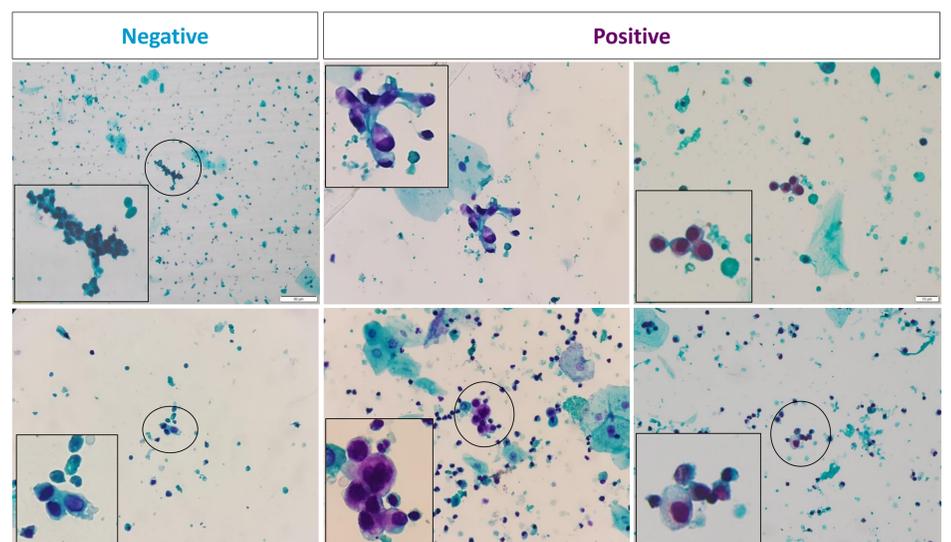


Figure 2: Negative and positive prostate samples stained using CellDetect® technology. Negative result by CellDetect®: cytoplasm of epithelial cells is stained in green and the nuclei in purple/green. Positive CellDetect® result in which the nuclei of the positive cells is stained in deep violet.

## Conclusions

CellDetect® proved to be a very sensitive method to detect PC. This test may support a prostate biopsy in a patient with an elevated PSA. However, a negative result does not obviate the need for a prostate biopsy. Our results warrant confirmation in a larger clinical study in patients without a known diagnosis of prostate cancer who are undergoing a prostate biopsy.