

# CellDetect®: an excellent staining test for accurate diagnosis of urine cytology

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## Background

Urine cytology is commonly used in conjunction to initial detection and continuous surveillance of bladder cancer patients. However, the test has poor sensitivity, especially for low grade tumours and relatively high frequency of Equivocal diagnoses (atypia or suspicious for malignancy) that limit its relevance. Urovysion FISH is done most often in conjunction with the urine cytology, to increase sensitivity.

As opposed to standard histochemical stains which only rely on morphology, CellDetect® uses both color and morphology to differentiate between normal and malignant cells. This color feature enhances the diagnostic accuracy across all cancer stages.

The objective of this study was to validate the routine use of CellDetect® in a cytopathology laboratory by comparing its performance to urine cytology and FISH-Urovysion, and to assess its potential to reduce the number of undetermined readings.

## Study Design

The study was performed in one pathological laboratory and included voided urine samples patients with haematuria or under surveillance for bladder cancer. The samples were processed into smears using ThinPrep® technique. For each sample, one slide was stained with Papanicolaou stain, one slide was stained with CellDetect® and, for chosen cases, Urovysion FISH was tested. Cystoscopy, biopsy and other clinical assessments were used as gold standard.

In this study there was a designed enrichment of undetermined cases, meaning, atypia and suspicious readings in standard cytology.

## Sample Cases

### Case 1

Confirmed by cystoscopy as low grade Urothelial Cell Carcinoma.

Standard cytology reading was negative and CellDetect® reading was positive.

PAP

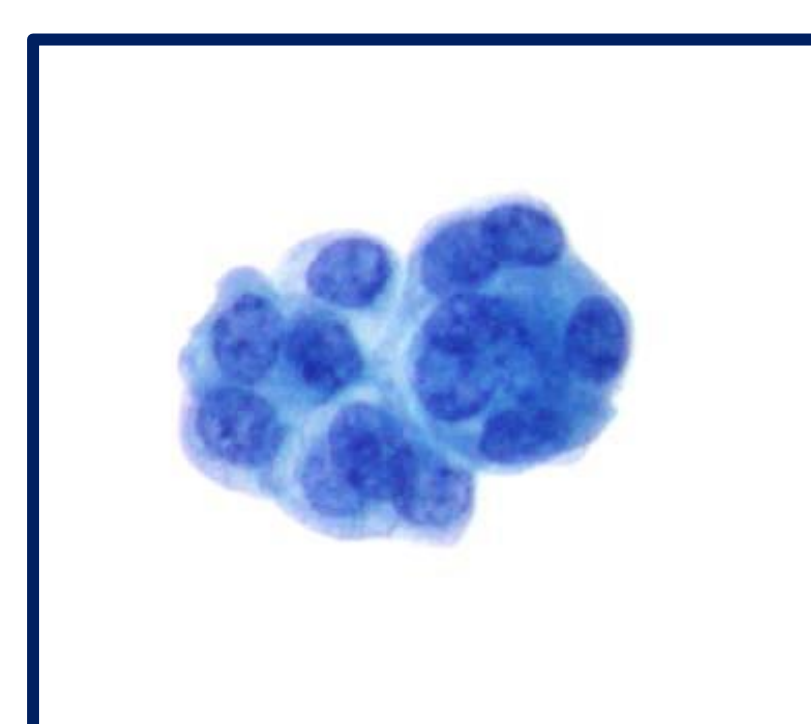
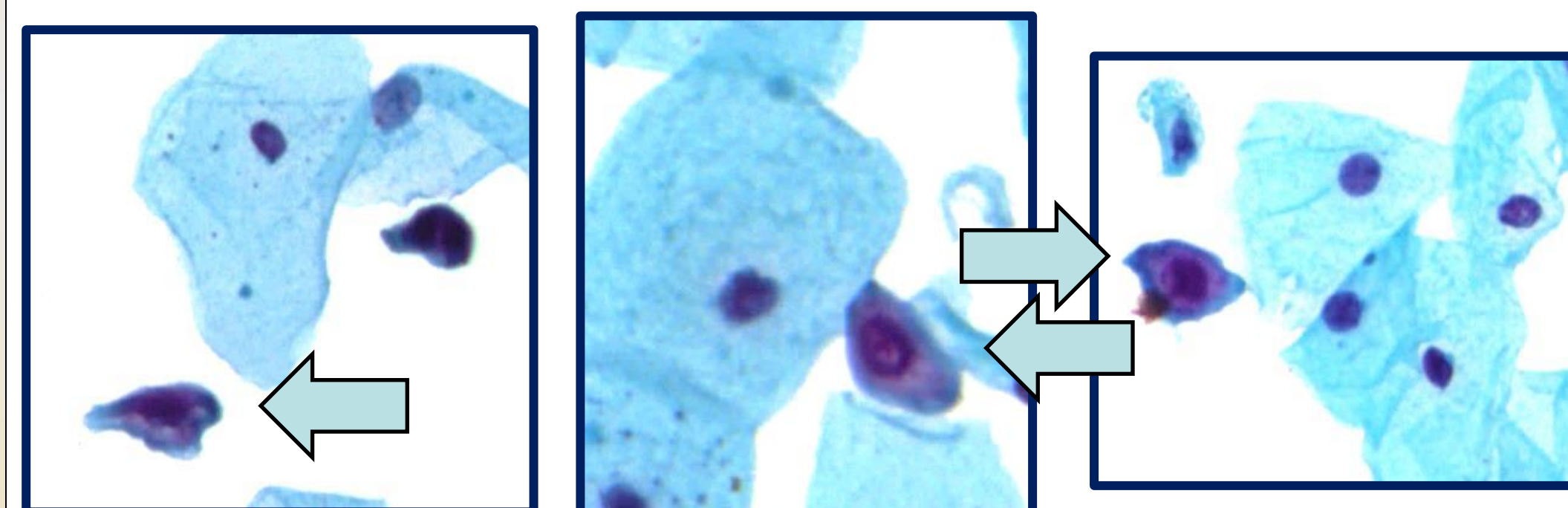


Image of a cluster from a PAP slide showing morphologically abnormal/dysplastic cells that were missed by the reviewer

CellDetect®



Images from a CellDetect® slide showing moderate altered cells, highlighted by a positive stain.

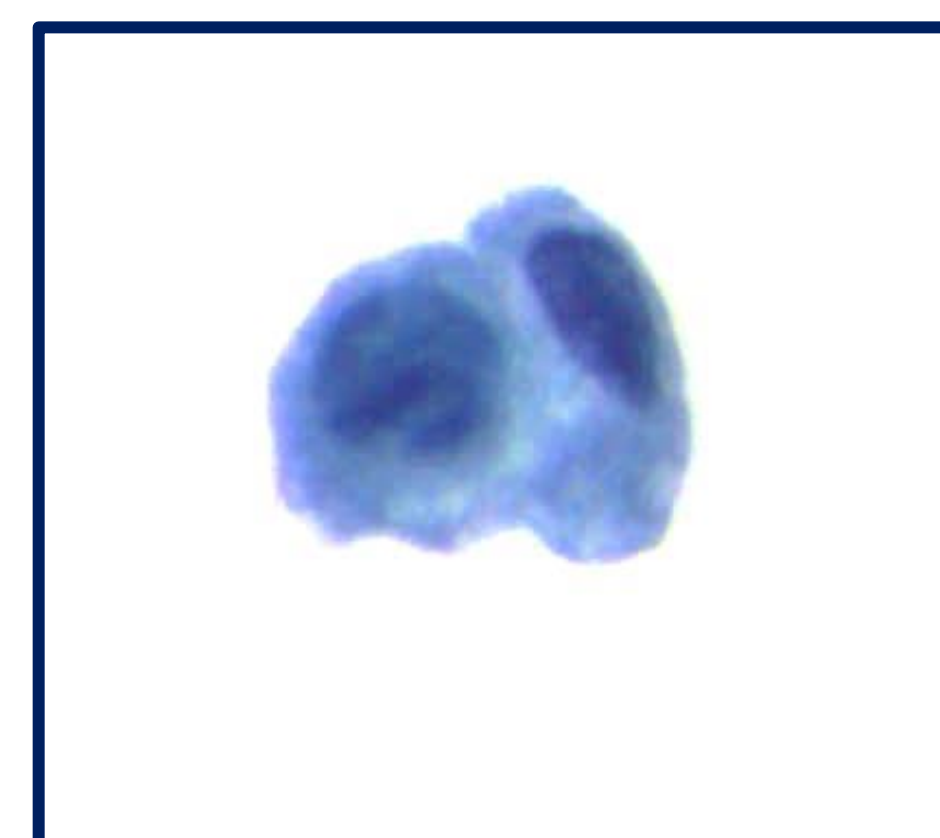
### Case 2

Confirmed by cystoscopy as low grade Urothelial Cell Carcinoma.

Standard cytology reading was atypia, Urovysion FISH reading was negative.

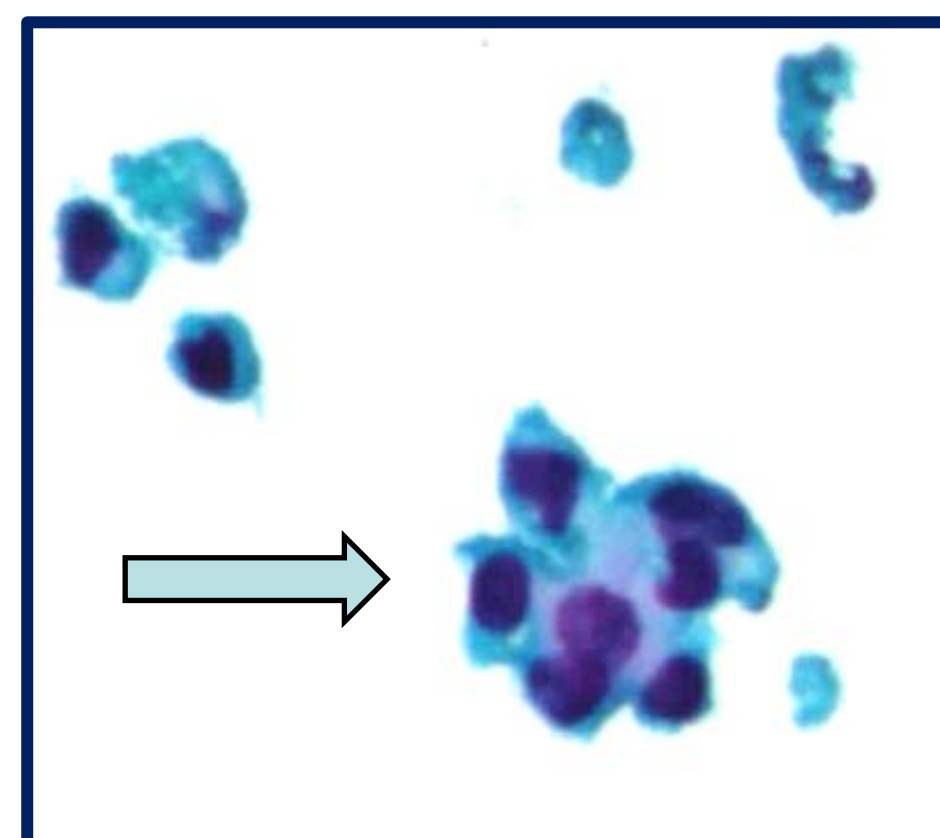
CellDetect® reading was positive.

PAP



PAP image showing moderate morphologically altered cells

CellDetect®



CellDetect® image showing moderate altered/dysplastic cells with a positive stain

All images shown above were taken at 40x magnification

## Results

67 urine samples were tested for CellDetect® and standard cytology (data is shown in fig.1).

CellDetect® is a platform that uses a metabolic signature to differentiate between benign and neoplastic cells which makes it a pan-cancer test. Since this study is aimed to detect Bladder cancer, 4 Patients diagnosed with other cancers were excluded from the final statistics.

Out of these 4 patients one had kidney TCC and three others had prostate cancer (3 out of those 4 patients were positive by CellDetect®)

The performance of the tests were computed based on cases with determined readings by PAP (fig.2) and undetermined PAP readings (fig.3 and fig.4).

2 cases initially considered as false positive readings by CellDetect® are counted as true positives after they were confirmed as positives by gold standard within a year of follow up.

Total	67
Positive	17
Negative	46
Excluded	4

**Figure 1: Diagnostic results by Gold Standard** -Gold standard used for this study was cystoscopies, biopsies and other clinical assessments

	Standard Cytology	CellDetect®	FISH
TN	23	35	18
TP	3	14	9
FN	4	0	6
FP	1	6	9
<b>SENS</b>	<b>43%</b>	<b>100%</b>	<b>60%</b>
<b>SPEC</b>	<b>96%</b>	<b>85%</b>	<b>67%</b>
Total	31	55	42

**Figure 2: Test Performance - Determined readings by standard cytology.**

	Standard Cytology	CellDetect®	FISH
Determined	31	55	42
Undetermined	32	7	4
<b>% of undet.</b>	<b>50 %</b>	<b>11%</b>	<b>9%</b>
Total	63	62	46

**Figure 3: Total undetermined cases** – One CellDetect® slide was inadequate and therefore was removed from final statistics

n=32	CellDetect®	FISH
TN	15	12
TP	9	7
FN	0	3
FP	3	7
und	4	2
<b>SENS</b>	<b>100%</b>	<b>70%</b>
<b>SPEC</b>	<b>83%</b>	<b>63%</b>
TOTAL	31	31

**Figure 4: Undetermined cases by standard cytology analysis** - One CellDetect® slide was inadequate and therefore was removed from final statistics

## Conclusions

CellDetect® showed to be a reliable test with performance of 100% sensitivity and 85% specificity. This study successfully shows a reduction of about 80% in undetermined readings. Equivocal diagnoses are common in standard urine cytology, hence, limiting the relevance of standard urine cytology in diagnosis of bladder cancer. Moreover, CellDetect® correctly classified 80% of the cases that were concluded as undetermined by standard cytology.

In total 10 (16%) cancer cases confirmed by gold standard, were not recognized by standard cytology, while they were correctly diagnosed by CellDetect®.