



CellDetect[®] improves performance of bladder cancer diagnosis compared to standard cytology and U-FISH

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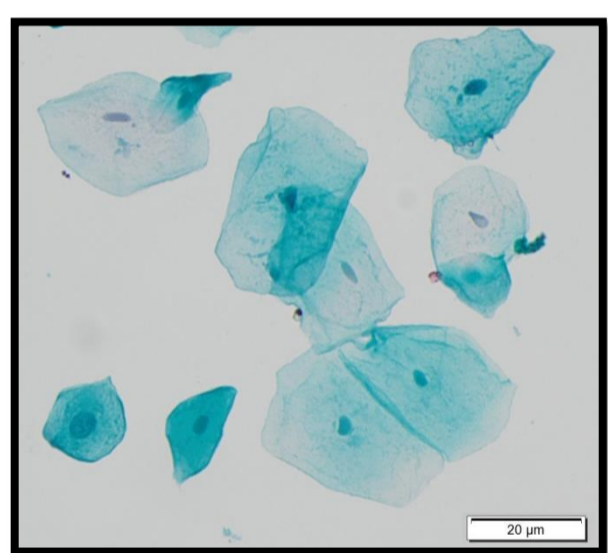
Introduction

Bladder cancer (BC) has become one of the common cancers globally, ranking 5th among the most frequently diagnosed cancers in Europe, with about 124,000 new cases annually as estimated by the International Agency for Research on Cancer (IARC). In addition, due to the high recurrence rates of the disease, rigorous, frequent and long-term surveillance is necessary.

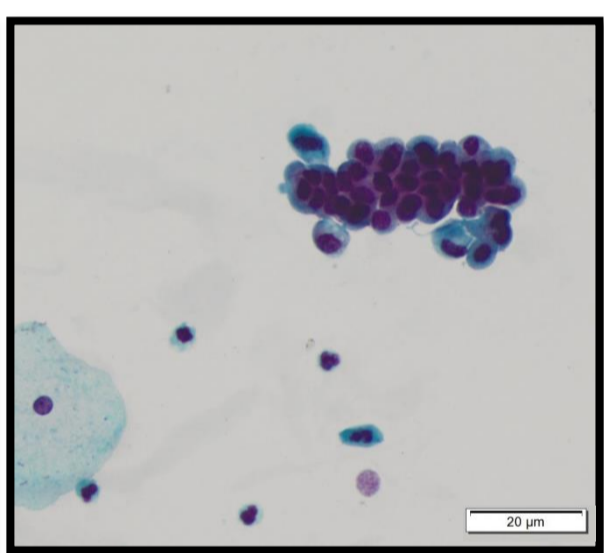
The current methods used for preliminary diagnosis and surveillance of BC recommended by the European guidelines include standard urine cytology and cystoscopy. Urine cytology present high specificity >90%. Nevertheless, cytology weaknesses are low sensitivity and high rate of undetermined readouts (i.e. "atypia" or "suspicious") which limits its value. Cystoscopy is considered gold standard (GS) however present low performance in detection of flat lesions. In light of these limitations, two commercially available tests may act as an ancillary diagnostic tool to aid in BC diagnosis: UroVysion FISH test (U-FISH) and CellDetect[®].

CellDetect[®] test is a unique histochemical stain enabling color and morphological discrimination between malignant and benign cells based on differences in the metabolic signature.

This study summarizes the performance of the PAP, U-FISH and CellDetect[®] compared to GS in BC diagnosis.



Negative urine smear



Low grade urine smear

Images of urine smears stained by CellDetect[®]: Benign nuclei of epithelial cells are stained in green / purple while dysplastic cells exhibiting deep violet, hyperchromatic nuclear stain

Objectives

Demonstrating the value of CellDetect[®] as an ancillary cytopathologic test for BC diagnosis in the routine laboratory setting, by comparing its performance to that of commonly used testing methods; standard urine cytology and the U-FISH test.

Methods

Voided urine samples were collected from patients with hematuria or patients under BC surveillance.

For each sample two liquid base slides were prepared, one was stained in standard urine cytology stain (i.e. Papanicolaou stain - PAP) and the second was stained with CellDetect[®]. In most cases, specimens were also prepared for U-FISH testing.

CellDetect[®] and PAP slides were reviewed blindly by pathologists under bright light microscope.

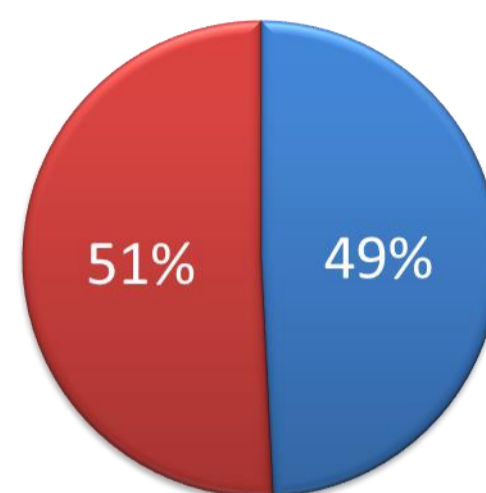
Results from all three tests were compared to GS confirmed by biopsy / cystoscopy/ acceptable clinical assessments.

Of note that a intended enrichment of PAP cases which received "atypia" or "suspicious for malignancy" reports was designed.

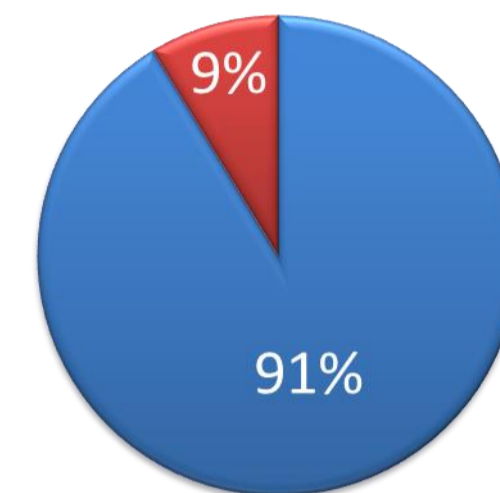
Results shown for this cohort are of 12 months follow up.

Results

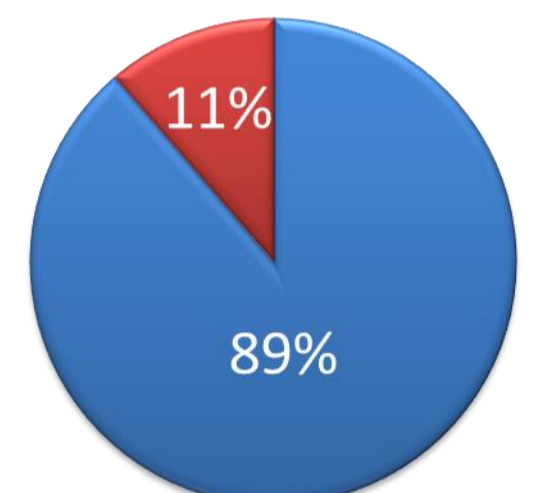
Standard Cytology



U-FISH



CellDetect



■ Determined ■ Undetermined

Determined vs. undetermined reading in CellDetect[®], standard cytology and U-FISH

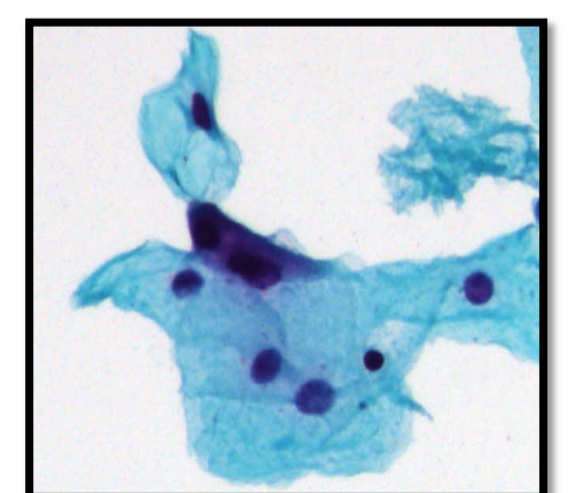
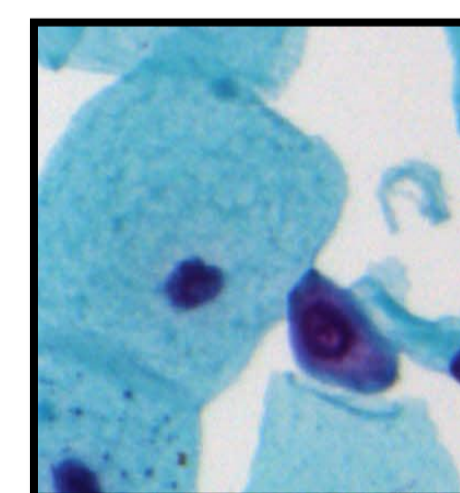
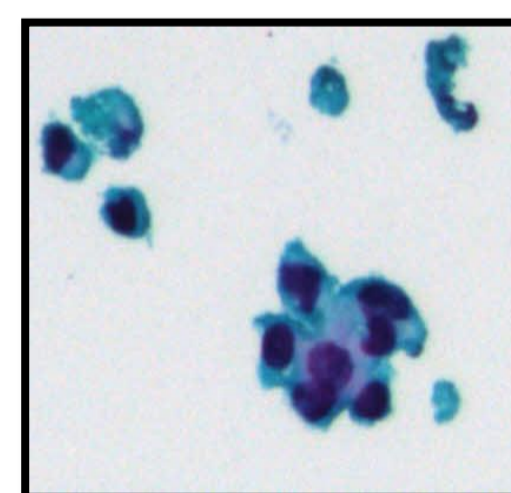
A total of 63 urine samples were tested in the study, of those 17 samples were positive and 46 samples were negative. All samples were tested for standard urine cytology, 62 for CellDetect[®] and 46 of the samples were also tested for U-FISH. CellDetect[®] and U-FISH determined readings exhibit similar performance with 89% and 91% respectively while with standard cytology determined readings where only 49%.

	Standard Cytology	U-FISH	CellDetect [®]
Sensitivity	43%	60%	100%
Specificity	96%	67%	85%
No. of cases	31	42	55

Table 1: Test performance of the modalities were computed based on the cases with determined readings.

	U-FISH	CellDetect [®]
Correct diagnosis	61%	80%
Incorrect diagnosis	23%	10%
Undetermined	6%	10%

Table 2: Standard cytology undetermined readings analyzed by CellDetect[®] and U-FISH. 80% of cases were correctly diagnosed by CellDetect[®] while with U-FISH 61% of cases received correct diagnoses.



Images representing CellDetect[®] slides. The presented cases were stained positive by CellDetect[®] however were missed by PAP. GS results confirmed the cases as low grade tumors. The images demonstrate moderate dysplastic cells highlighted by CellDetect[®]. Positive stain is indicated by hyperchromasia and a deep violet nucleus. Normal cells are stained with a purple nucleus and green cytoplasm.

Conclusions

- This study highlights the increased clinical relevance of urine cytology using CellDetect[®] as an ancillary test for detection of bladder cancer.
- The results demonstrate increased sensitivity of CellDetect[®] by 57% as compared to PAP.
- Particularly, using CellDetect[®] reduced the undetermined readings of PAP by 80%.
- Furthermore, CellDetect[®] positively identified 10 cancer cases confirmed by gold standard missed by standard cytology (16% of all cases).