Improved detection of urothelial carcinoma in cytology smears by using CellDetect® innovative staining.

Jacob Bejar[1]; Marina Zlotnik[1]; Ilan Bejar [2]; Sarel Halachmi[2]; Masarwe Ismail[2]; Kohava Biton[2]; Chen Yoffe [3]; Ofer Nativ [2]

(1) Department of Pathology, Bnai Zion Medical Center, Haifa, Israel; (2) Department of Urology, Bnai Zion Medical Center, Haifa, Israel; (3) Micromedic Technologies Ltd., Tel Aviv, Israel

Background

Accurate detection of urothelial carcinoma (UC) may be challenging, particularly in cases where cytomorphologic features overlap with those of non-neoplastic changes such as low-grade (LG). CellDetect histochemical stain uses a color feature to highlight neoplastic cells in urine specimens.

Blinded study has shown that this color feature significantly improves sensitivity when compared to standard cytology. The objective of this study was to confirm those findings in routine clinical settings, and to compare CellDetect to UroVysion FISH (FISH) performance.

Design

Patients undergoing routine cystoscopy surveillance or TURBT were enrolled. Voided urine samples were processed into two slides. The Slides were stained by CellDetect and standard cytology stain (PAP). A subset of samples was also processed for FISH testing (UroVysion). A Cytopathologist diagnosed the two slides and a trained specialist diagnosed the FISH slides. All results were compared to gold standard (biopsy/cystoscopy).

Results

The study included 107 patients: 66 negative and 41 positive. All cases were diagnosed by PAP, 101 cases by CellDetect, and 33 cases by FISH.

The overall sensitivity of CellDetect® was significantly higher than PAP and 20% higher than FISH. The performance of the three methods (sensitivity and specificity) is summarised in figure 1.

CellDetect® accuracy compared to that of PAP and FISH Urovysion is summarized in Table 1. Notably, a higher number of cases was correctly classified by CellDetect®, of both high- and low- grade bladder cancer tumors, than PAP and FISH Urovysion.

Tests Performance

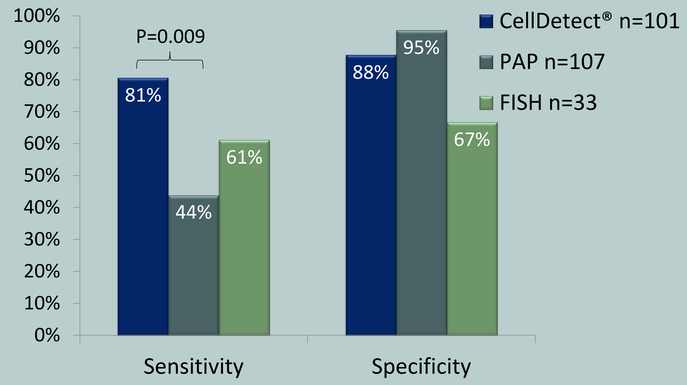

Fig 1: Tests Performance. Overall sensitivity and specificity of CellDetect®, PAP and FISH

Tests Sensitivity by Grade and Stage

	CellDetect®	PAP	FISH
LG + PUNLMP	68%*	25%*	54%
HG	94%	71%	80%
NMIBC	76%**	38%**	61%
MIBC	100%	71%	N/A

Table 1: CellDetect® sensitivity exceed PAP and FISH sensitivity throw all grades and stages (significantly higher *p=0.005; ** p=0.001). Low grade (LG). Papillary urothelial neoplasm of low malignant potential (PUNLMP). High grade (HG). Non-muscle-invasive bladder cancer (NMIBC). Muscle-invasive bladder cancer (MIBC).

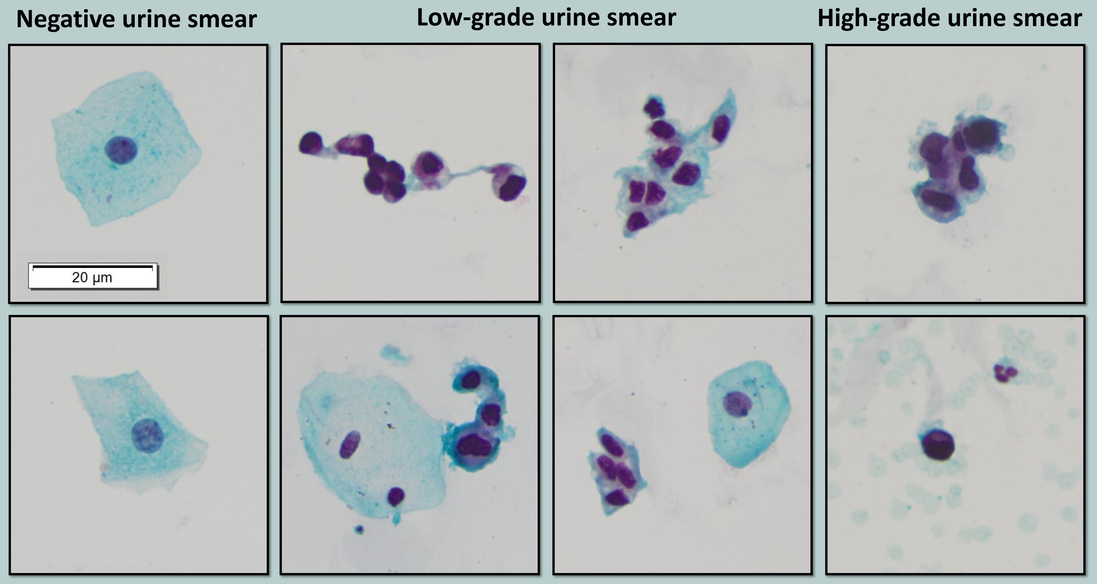

Fig. 2: Images of urine smears stained by CellDetect®: Normal epithelial cells nuclei are purple and the cytoplasm is green. Dysplastic cells exhibiting hyperchromatic violet nuclei and the cytoplasm may be green or pinkish (magnification x40)

Conclusions

The study shows that CellDetect® was almost two times more sensitive than standard cytology and was also higher than FISH, by 25%.

The overall higher sensitivity of CellDetect® was achieved while maintaining relatively high specificity results.

The advantages of CellDetect® over standard cytology were particularly evident in NMIBC and LG tumours.