

Performance of an innovative urine-based biomarker for the monitoring of bladder cancer recurrence

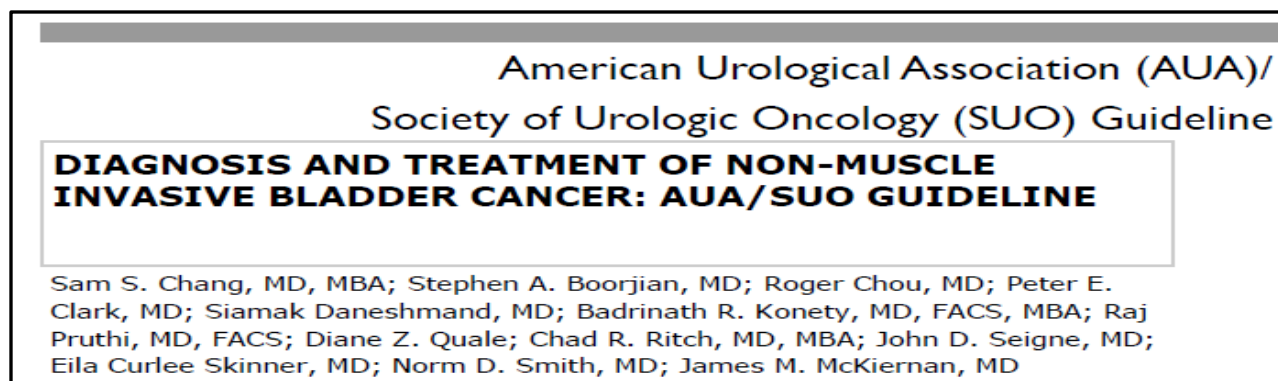
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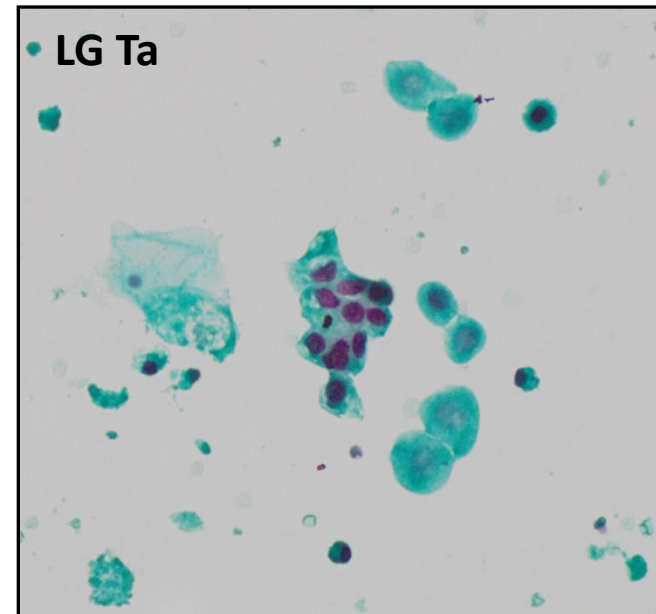
Background

- Voided urine cytology is recommended as an adjunct to cystoscopy in the monitoring of intermediate or high-risk patients
- Urine cytology is not recommended for the routine surveillance of patients with history of low-risk bladder cancer



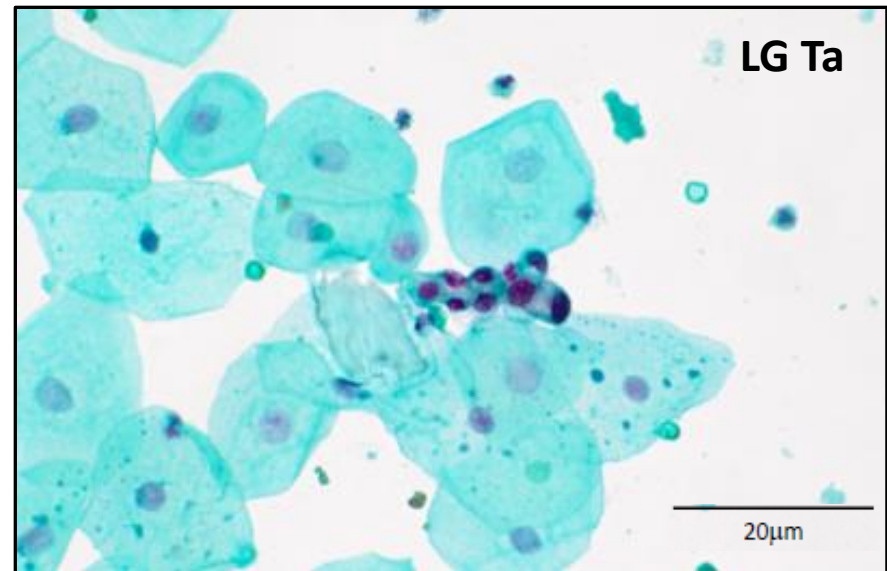
Detection of low-grade UCC – an unsolved challenge

- Extensive overlap between cytomorphological features of low-grade UCC and non-neoplastic changes compromises the use of standard urine cytology stain in the monitoring of low-risk patients
- To address this shortcoming, we have used an innovative urinary marker (CellDetect[®]) to detect low and high grade malignant cells



What is CellDetect[®] staining technology?

- CellDetect[®] is an histochemical stain composed of a unique plant extract and generic dyes
- The active component of the plant extract interacts with proteins found in malignant cells, thus leading to their labeling with the red dye
- Benign epithelial cells are counter-stained in green



Results of a multi-institutional blinded study performed in a Central Lab

- 217 voided urine specimens from patients monitored for UCC
- Overall sensitivity was 84% and sensitivity for detecting LGNMIBC was 78% compared to 33% for standard urine cytology ($p \leq 0.05$)
- Specificity in patients undergoing routine surveillance by cystoscopy was 84%
- 21% of patients with positive CellDetect[®] and negative gold standard relapsed within the next 9 months compared to 5% in the CellDetect[®]- negative group

Study objective

The objective of the present study was to evaluate the reproducibility and performance of the stain in an independent cytology laboratory.

Methods

- Voided urine samples were collected before intervention from two cohorts of patients monitored for UCC:
 - 1st - patients undergoing routine F-U cystoscopy
 - 2nd - patients scheduled for TURBT
- Urine samples were processed into two smears and each slide was stained with either CellDetect[®] or standard urine cytology
- Both specimens were observed by a Cytopathologist blinded to the final diagnosis
- Results were compared to the gold standard (biopsy for positive cases and biopsy or cystoscopy for negative cases)

Results - case distribution

- 73 urine specimens were obtained from patients monitored for UCC between July 2015 and March 2016
 - 51 cases proven negative by either normal cystoscopy (n=48) or non-malignant histological findings (n=3)
 - 22 cases proven positive by histology including 11 low-grade tumors and 11 high-grade tumors

Results – overall test performance

	n	CellDetect [®]	Standard Stain	P-value
Sensitivity	22	82%	59%	p<0.05
Specificity	51	86%	94%	NS

Results – test sensitivity per stage/grade

Stage/grade	n	CellDetect®	Standard Stain
LG	11	73%	45%
HG	11	91%	73%
Ta, T1, Tis	14	71%	50%
T2 and up	7	100%	71%

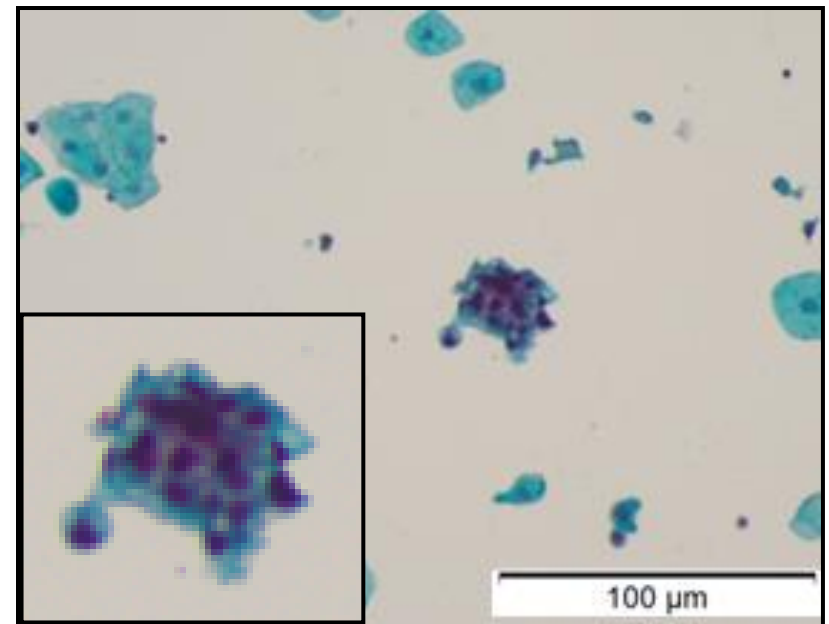
CellDetect® ruled out malignancy in 5 out of 7 cases classified as “undetermined atypia” by standard urine cytology stain

Study limitations

- Long term follow-up of patients with positive CellDetect[®] and negative gold standard was not available to confirm possible cases of early detection
- Patients with catheters, neobladder, ileal conduit or kidney stones were excluded from the study and the effect of these interferences should be assessed in future investigation

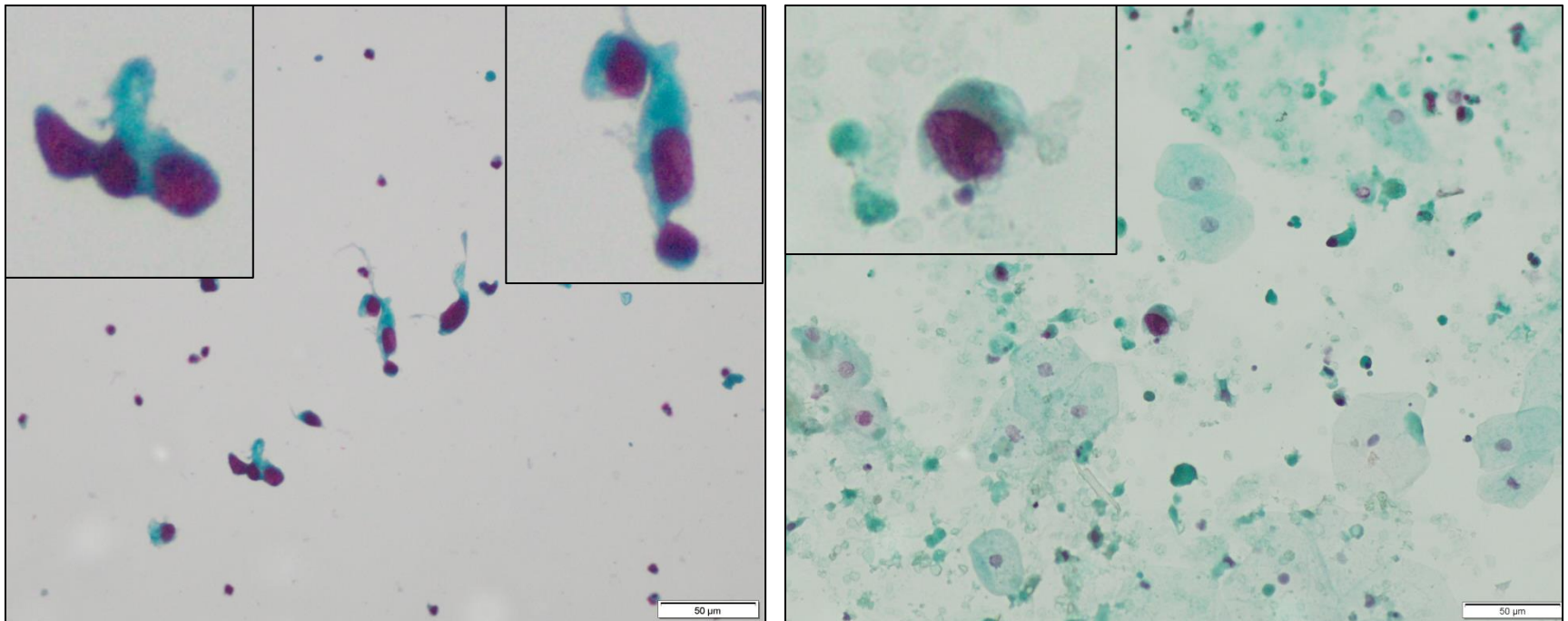
Conclusions

- This study validates the reproducibility and performance of CellDetect[®] in the settings of an independent cytology laboratory (“real life”)
- It confirms the ability to identify low-grade bladder cancer cells in urine specimens with high sensitivity
- The study confirms the usefulness of the marker in the ruling out of malignancy in undetermined atypia



Conclusions

- The clinical implications of CellDetect® in serving as an efficient diagnostic tool in bladder cancer surveillance warrants further investigation





Thank You