

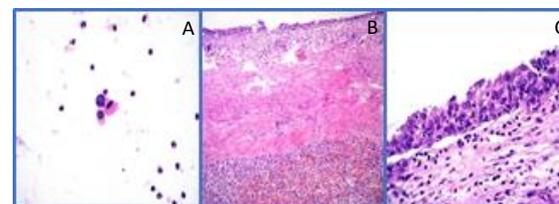
# Application of The Paris System to specimens from upper tract urothelial tumors: correlation with histology

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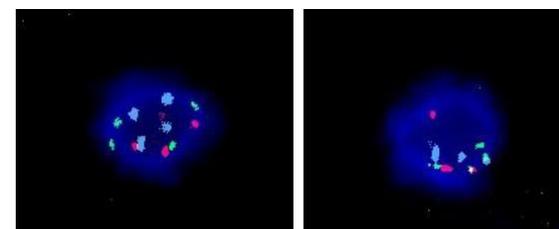
**Objective:** Urine cytology specimens are essential for screening high-grade urothelial carcinomas, and detecting of the lesion from upper urinary tract (UUT) is more challenging. The Paris System for Reporting Urinary Cytology (TPS) was developed to provide clear cytomorphologic criteria for urine cytology specimens. To detect the correlation between the surgical biopsy diagnosis and TPS diagnosis in upper urinary tract carcinomas.

**Method:** From 2013 to 2018, voided urine liquid-based cytology samples corresponding to 180 biopsy-proven cases (153 high-grade carcinomas, 25 low-grade carcinomas, and 2 benign lesions), were reclassified by the two experienced cytopathologists using TPS. Diagnostic agreement and sensitivity for the nomenclature system was measured. Six atypical urine cytology samples are sent for multiprobe fluorescence in situ hybridization (FISH) test.

**Results:** None of the cases with a cytology of low-grade urothelial neoplasm was found to have a high-grade urothelial carcinoma (HGUC) on biopsy. Among the 25 atypical urothelial cells (AUC) cytology cases, the histology is heterogeneous (one benign, twelve low-grade lesions, and twelve HGUCs). The risk of HGUC for each cytological diagnostic category are 13.6% for negative for HGUC, 48% for AUC, 0% for low-grade urothelial neoplasm, 93.5% for suspicious for HGUC and 100% for positive HGUC. When we considered cytology cases with suspicious or positive for HGUC interpretations as positive, the performance of TPS in predicting high grade urothelial carcinoma on histology had values of: 83% sensitivity, 96.3% specificity, 99.2% positive predictive value and 50% negative predictive value. Four of six AUC cytology cases tested positive on UroVysion, and one was suspicious positive. All the five cases were proven HGUC by histopathology. The negative case tested on FISH was a low grade urothelial carcinoma by histology.



All specimens from the same patient. A: atypical urothelial cells from voided urine (ThinPrep, 400x). B-C: Urothelial cells proliferation overlying a clear cell renal cell carcinoma from total right nephrectomy (B: 400x, C: 400x).



High grade urothelial carcinoma from voided urine :  $\geq 25$  analyzed cells, gains for CSP3, CSP7 and/or CSP17,  $\geq 12$  cells show loss for p16, FISH result is positive.

Cutoff point	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Kappa value	Asymp. Std. Error
Positive for HGUC	88.20%	50%	99.37%	4.55%	0.064	0.072
Suspicious and Positive for HGUC	83.00%	96.30%	99.22%	50%	0.574	0.069
AUC and above	85.62%	48.15%	90.34%	37.14%	0.301	0.089

**Conclusion:** As the only noninvasive diagnostic tool, voided urine was an effective means in the detection of UUT carcinomas. The use of TPS in evaluating UUT cytology specimens was specific and sensitive in identifying patients with HGUC, and FISH can be helpful on the cases which are diagnosed with AUC.

