

EVALUATION OF DNA CONTENT AND CHROMATIN COMPLEXITY AS STRATIFICATION PARAMETERS TO ASSESS SEVERE UROTHELIAL ATYPIAS IN URINARY CYTOLOGY SPECIMENS OBTAINED IN A PATHOLOGY REFERENCE LABORATORY. Gerard J. O'Dowd, Garry M. Marley, Michael Bacus, Roberto Orozco, David B. Durand, Robert W. Veltri, Oklahoma City, OK; [presented by Dr. O'Dowd]

Diagnosis of urothelial atypia remains a prognostic dilemma for the urologist and cytopathologist. There is a need for improved objective cellular pathology methods to address this deficiency. This study involved the evaluation of 58 patients having a history of bladder cancer and exhibiting severe urothelial atypia diagnosed by a single uropathologist. These patients were monitored over a period of about 24 months for evidence of persistence, regression, or progression of their cytologic abnormalities. The latter are defined as follows: persistence = no change in atypia status; regression = a significant reduction in the cytologic findings to negative or mild atypia; progression = increase in cytologic abnormalities to dysplasia or carcinoma. For the purposes of this study severe atypia was defined as urothelial changes that manifested some but not all the features of dysplasia using both PAP and Feulgen stained 25 mm filter cell imprints. The cytomorphologic abnormalities assessed included cellularity, nuclear size, membrane irregularity and chromatin texture, as well as N/C ratio to differentiate severe atypia from dysplasia. The Feulgen stained nuclear images were then captured using a CAS-200 image analysis system equipped with DNA ploidy and cell morphometry software. The DNA ploidy patterns were assessed by at least two investigators and classified as normal, out of normal range, and abnormal. Nuclear morphometry involved the selection of four key Markovian chromatin features, and a analysis of their complexity using two dimensional comparison plots. There was a statistically significant correlation (Chi Square analysis) between normal DNA content and regression ( $p=0.022$ ); out of normal range DNA content and persistence ( $p=0.018$ ); and abnormal DNA content and progression ( $p=0.05$ ). Chromatin texture complexity analysis confirmed these observations. These preliminary results suggest that quantitative image analysis may provide adjunctive prognostic and diagnostic information of use in the monitoring of patients exhibiting urothelial nuclear atypias.