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**Combining quantitative histomorphometry with NF-κB/p65 nuclear localization- A better predictor of biochemical recurrence in prostate cancer patients**

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Though the approach of risk determination possess major uncertainty, it is the major basis of clinical management decisions in prostate cancer. Only limited tools are available to understand the risk of disease recurrence and guide the treatment decision process. Computer-aided quantitative histomorphometric analysis has emerged as a powerful computing tool to identify, characterize, and quantitate histologic features of tissues beyond human visual capabilities. Several quantitative features can be assessed, such as precise numeric measurements pertaining to the spatial arrangement and architecture of nuclei, shapes of nests and nuclei, and nuclear texture. This technology has proven to be useful for the detection of cancer in tissue sections and also for predicting tumor biology and clinical outcome in cancer patients. Utilizing a combination of synergistic strategy of quantitative histomorphometry and biomarker expression of NF-κB/p65 from prostate tissue specimens, we sought to fuse structural and functional information from morphological and molecular markers to better characterize disease progression improving prediction of biochemical recurrence (BCR). We utilized radical prostatectomy specimens (n=23) for feature extraction from 15 patients without BCR and 8 patients who experienced BCR (PSA > 0.2 ng/ml) within two years of surgery. Digitized H&E slides were annotated for a representative cancerous region, glands were automatically segmented, and 216 features of gland architecture, shape, and orientation disorder were extracted. Nuclei were automatically segmented from NF-κB/p65 stained slides. Based on digitally calculated stain optical density, every nuclei pixel was classified as either negative or weakly, moderately, or strongly positive for NF-κB/p65 staining. H&E features alone in leave-one-out cross validation with a naive Bayes classifier was applied, using the top two features by t-test in every fold, to obtain a recurrence probability and repeated for NF-κB/p65 features. Analysis demonstrate that the three most predictive H&E features were all gland orientation disorder features. The top NF-κB/p65 feature was percentage of nuclei pixels positive for staining. Accuracy predicted was 78% with H&E features alone, 74% with NF-κB/p65 features alone, and 87% in the aggregate model. Taken together, our results demonstrate that fusing nuclei NF-κB/p65 and gland morphology information allows for functional and morphologic characterization of prostate cancer, potentially allowing for improved risk characterization and prognosis prediction in prostate cancer patients.