Digital Microscopy Evaluation of Cellular proliferation, Vascularization, and Gleason grade.

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ABSTRACT

Background: Histologic grade (Gleason grade) is the strongest, single factor which distinguishes clinically aggressive from indolent prostate cancer. Yet a robust and credible biologic explanation for the different growth patterns driving the grading system has proven elusive. We hypothesize that Gleason grade results from a dynamic interaction between cancer associated stroma with malignant epithelial cells. Here, we implement an automated approach based on digital microscopy to study expression of two markers chosen to represent epithelial (MIB1) and stromal (CD31) compartments in prostate cancer samples obtained following radical prostatectomies. Methods: Images were obtained from immunohistochemistry (IHC) sections representing low-, intermediate-, and high-grade prostate cancer stained for expression of MIB-1(proliferation) and CD31 (vascularity). An automated workflow was developed using a training set of regions of interest (3 lower power field equivalents/ section) representing MIB1 and CD31 expression in sequential tissue sections. Next, the automated approach was used to study co-localized expression of MIB1 and CD31 in digital images at 40X equivalent magnification across an entire slide representing a standard formalin-fixed paraffin embedded block. Relationships between MIB1, CD31, and Gleason grade were explored. Results: Using the training data set, we confirmed the known association between MIB1 and Gleason grade using our automated approach. CD31 expression was more heterogeneous across samples and did not vary with Gleason score in this cohort. Interestingly, the MIB1/CD31 ratio was significantly increased in high (≥ 8) versus low/intermediate (≤7) samples when assessed in the training set as well as the whole slide images. Discussion: This work establishes a framework for automated image analysis of high-resolution digital microscopy images based on standard IHC techniques. Our preliminary results points towards a finding that proliferation (MIB1 expression) is relatively less dependent on vascularity (CD31 expression) in high-grade prostate cancer. This basic approach can be expanded to study the expression and distribution of multiple epithelial and stromal markers using readily available IHC-based assays with the eventual goal of gaining greater understanding into the biologic basis for high-grade prostate cancer.

Conflicts of Interest: None

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