Risk Stratification of Prostate Cancer in Needle Biopsy Specimens: Utilization of a Multi-gene FISH Panel

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Background: In an effort to lessen overtreatment of prostate cancer, further risk stratification on needle biopsy specimens can be critical for patient management. Men with low-risk disease are candidates for active surveillance. Currently, the most important feature for risk stratification is Gleason score; however, sampling error in the needle biopsy procedure results in a significant underestimation of risk in harboring a Gleason grade 4 (Group 2 or 3). The objective of this study was to use genomic features associated with significant prostate cancer previously identified by massively parallel mate-pair next generation sequencing (NGS), and create a model now using fluorescence in situ hybridization (FISH) that could be applied to needle biopsies to improve risk stratification.

Methods: FISH probes for six genomic alterations associated with significant prostate cancer were applied to 150 contemporary consecutive needle biopsy specimens of men who underwent radical prostatectomy (RP), and a model was constructed that predicted for men with Gleason score (GS) 6 (Group 1) on needle biopsy, the probability of GS 7 and higher (Group ≥2) in the RP specimen. The final outcome measured was the predicted probability of harboring a significant cancer or GS > 7 (Group ≥2) in the prostate gland based on a derived formula from FISH analysis of single core needle biopsies. Concordance measures were created using an elastic net model.

Results: The application of these probes to needle biopsy specimens confirmed that a model composed of PTEN, CHD1, ASAP1 and HDAC9 was predictive of upgrading (AUC 0.788) from GS 6 on needle biopsy to GS ≥ 7 in RP specimens. The AUC on the biopsies was less than that on earlier discovery and validation sets likely related to inter-tumoral heterogeneity and sampling bias from biopsies.

Conclusions: Use of this model could be clinically useful in risk stratification for patients considering active surveillance for prostate cancer by separating those GS 6 (Group 1) on biopsies into “lower” or “higher” risk.

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