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Cell Cycle Progression (CCP) Score Significantly Predicts PSA Failure After EBRT

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Purpose/Objective(s): Accurate risk stratification is crucial to aid appropriate decision making in localized prostate cancer. To address this need, we have developed the Cell Cycle Progression (CCP) score, based on the collective gene expression of 31 cell cycle genes. To date, this score has been shown to not only predict BCR after prostatectomy, but also prostate cancer specific mortality in men undergoing observation in the United Kingdom. However, the value of this score based upon needle biopsies in men undergoing primary EBRT is untested.

Materials/Methods: The CCP score was evaluated retrospectively in 152 patients treated with EBRT. Inclusion criteria were disease diagnosis from 1991 to 2006 and available biopsy tissue. Approximately half of the cohort was African-American. CCP score was derived from diagnostic biopsy. Outcome was time from EBRT to biochemical recurrence (BCR) using Phoenix definition, and median follow-up for patients without BCR was 5 years. Of the 152 initially selected patients, 6 were excluded due to delayed treatment (> 2 years from diagnosis) and 5 generated poor quality CCP scores, leaving 141 patients for analysis. Association with outcome was evaluated by CoxPH survival analysis and likelihood ratio tests.

Results: Patient data was censored at 5-years of follow-up, 16 patients (11%) had BCR. The median CCP score was 0.12(IQR -0.43 to 0.66). In univariate analysis, CCP score was the most significant prognostic variable (p-value = 0.002). The hazard ratio (HR) for BCR was 2.71 (95% CI, 1.44, 5.09) for a one-unit increase in CCP score. In a predefined multivariate analysis that included Gleason score, PSA, and percent positive cores, the HR for CCP remained largely unchanged (HR per CCP unit 2.53 (95% CI, 1.14, 5.61; p-value = 0.019) demonstrating that CCP provides prognostic information that is largely not provided by clinical parameters. There was no evidence for interaction between CCP and any clinical variable, including ethnicity.

Conclusions: We have evaluated the prognostic utility of CCP score for predicting BCR after EBRT. The CCP score was strongly associated with BCR and provided prognostic information beyond what is available from clinical parameters. If these results are validated in a larger cohort, then CCP score could be used to select high-risk men undergoing EBRT who may need combination therapy for their clinically localized prostate cancer.

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Validation of a Genomic Classifier That Predicts Metastatic Disease Progression in Men With Biochemical Recurrence Post-Radical Prostatectomy

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Purpose/Objective(s): Almost 50,000 men per year will present with biochemical recurrence (BCR) following local treatment for prostate cancer. These men with rising PSAs as the lone indicator of recurrence present a management dilemma due to their varied outcomes, as only a proportion subsequently develop metastatic disease. Thus, there is a clear need to improve patient risk stratification in this context. Here, we evaluate a genomic classifier (GC) in men with BCR following radical prostatectomy (RP) for its ability to predict metastasis.

Materials/Methods: The 22-marker GC was validated in a prospectively designed case-cohort study of 1,010 clinically high-risk RP patients. Two hundred nineteen patients, including 85 who developed BCR at least 6 months post-RP were subjected to microarray analysis and GC scores were generated. Survival ROC curves, weighted Cox proportional hazards, and decision curves were used to compare the performance of the GC to Gleason score (GS), PSA doubling time (PSAdT) and time to BCR (ttBCR).

Results: Of the 85 patients with BCR after RP, 46% had a low GC score and 54% had a high score (using a pre-specified cut point of 0.4 identified during previous development of the GC panel.) GC scores significantly stratified men with BCR into those who would or would not develop subsequent metastasis. Forty percent of patients with a high GC score (versus 8% with a low GC score) developed metastasis at 3 years following BCR depending on GC score category, $p < 0.001$). The AUC (for prediction of subsequent metastases) was 0.82 (95% CI, 0.76-0.86) for GC, compared to 0.64 (0.58-0.70) for GS, 0.69 (0.61-0.77) for PSAdT and 0.52 (0.46-0.59) for ttBCR. In decision curve analysis, the GC had the highest overall net benefit, and in multivariable modeling with clinicopathologic variables, only GC ($p = 0.006$) and GS ($p = 0.046$) scores were significant predictors of metastasis.

Conclusions: When compared to clinicopathologic variables, the GC better predicted metastatic progression among men with BCR following RP. While confirmatory studies in additional patient populations are required, these results suggest that use of the GC can allow for better selection of men requiring intensification of therapy, such as the addition of androgen deprivation therapy to salvage radiation, at the time of BCR. These results also support the rationale for further efforts to identify genomic-based prognostic or predictive factors in patients treated with radiation therapy for prostate cancer.

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Serum Testosterone Changes in Patients Treated With Radiation Therapy Alone for Prostate Cancer on RTOG 9408

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Purpose/Objective(s): In light of studies suggesting that radiation therapy (XRT) may influence serum testosterone (ST) levels for patients treated for localized prostate cancer, we reviewed data on testosterone changes for patients treated with XRT alone on RTOG 9408.

Materials/Methods: Patients enrolled on RTOG 9408 (T1b-T2b, PSA < 20 ng/mL) were randomized between XRT alone and XRT plus 4 months of total androgen ablation. XRT consisted of either whole pelvic radiation therapy to 46.8 Gy plus a 19.8 Gy prostate boost for a total dose of 66.6 Gy (WPRT) or treatment to the prostate alone for a total dose of 68.4 Gy (PORT). Most patients received WPRT. Only patients with the