A 17-gene genomic prostate score (GPS) as a predictor of biochemical (BCR) and clinical recurrence (CR) in men with surgically treated intermediate- and high-risk prostate cancer (PCa).

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Background: The biopsy-based GPS (scale 0-100) is validated as an independent predictor of adverse pathology in men with low- and intermediate-risk PCa. We wished to examine the association of GPS with BCR and CR in higher-risk disease.

Methods: We performed exploratory analyses of data from a prior development study of radical prostatectomies from 441 men with AUA low-, intermediate- and high-risk disease, using a cohort sampling design (Klein et al. Eur Urol 2015). Multivariable Cox proportional hazards models were employed with the cohort sampling weights. Since these data were used in the selection of genes and coefficients for GPS, hazard ratios (HR) and other estimates based on GPS were corrected for regression to the mean (RM), and Storey's method was applied to hypothesis tests for GPS to control the false discovery rate (FDR).

Results: All estimates are RM-corrected. Broad, overlapping ranges of GPS values were observed across all AUA risk groups. GPS was strongly associated with BCR (HR 1.64 for 20 GPS units, p<0.001, FDR q-value < 0.1%) and CR (HR 2.79 for 20 GPS units, p < 0.001; FDR q-value < 0.1%), after adjusting for AUA risk group. Intermediate-risk patients with GPS > 40, who represented 41% of all intermediate-risk patients, had estimated 3-year BCR risk and 10-year CR risk similar to high-risk patients (Table). Conversely, high-risk patients with GPS≤ 40, who represented 63% of all high-risk patients, had a 3-year BCR risk and a 10-year CR risk similar to men with intermediate-risk disease. High-risk patients with GPS > 40 had 3-year BCR risk of almost 50% and 10-year CR risk of 35%.

Conclusions: GPS appears to provide improved risk stratification for BCR and CR in AUA intermediate- and high-risk PCa. These findings require confirmation in an independent cohort of patients.

RM-corrected 3-year biochemical recurrence risk and 10-year clinical recurrence risk for intermediate- and high-risk patients.

	Intermediate risk			**High risk**		
GPS group	Percentage of patients	BCR risk	CR risk	Percentage of patients	BCR risk	CR Risk
GPS ≤ 40	59%	15.7%	4.7%	63%	23.8%	8.5%
GPS > 40	41%	33.5%	16.9%	37%	47.8%	34.9%
All	100%	22.7%	9.6%	100%	32.9%	18.2%