A 17-Gene RT-PCR Prostate Assay: Clinical Experience in 33,000 Patients with Clinically Low-Risk Prostate Cancer

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INTRODUCTION AND OBJECTIVES

- Tissue-based molecular diagnostic assays are often used for the purpose of improving risk stratification for men with newly diagnosed prostate cancer.[1]
- The 17-gene Oncotype DX Genomic Prostate Score® (GPS™) assay is a biopsy-based gene expression assay specifically developed for clinically low-risk prostate cancer: NCCN® very low (VL), low (L), and favorable intermediate risk (FIR).
- The GPS assay has been clinically validated to predict the risk of adverse pathology (AP) at time of diagnosis, as well as the likelihood of metastasis or prostate cancer death within 10 years.[2]
- The GPS result is combined with baseline NCCN risk to stratify a patient to a 'post-GPS' risk group which aligns with the overall risk parameters of the corresponding NCCN classification.
- Here, we report the Genomic Health Clinical Laboratory experience for samples submitted after prostate cancer guidelines and GPS report were updated in May 2017 to include favorable and unfavorable intermediate groups.

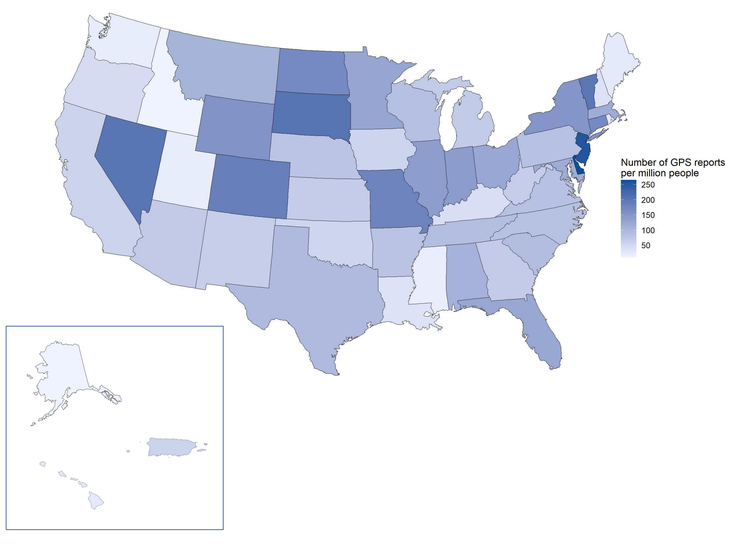
METHODS

- Results are based on 32,430 US commercial samples submitted to the Genomic Health Clinical Laboratory from May 2017 through May 2019.
- All samples included in these analyses passed pathology review and RT-PCR quality measures and had data on submitted NCCN risk group.
- GPS result (scale 0-100) was calculated based on the validated algorithm with 12 prostate cancer-related genes across four pathways and five reference genes.[2]
- Physicians provided clinicopathologic characteristics when they ordered the assay, which were descriptively summarized.
- The change in risk classification from the submitted NCCN risk group to the post-GPS assigned risk category is reported here.

RESULTS

Figure 1. GPS Assay Use in the US, Normalized by State Population

The data are presented as number of GPS reports per 1,000,000 people in each state. Population estimates are based on 2019 data from US Census Bureau.



Conclusions/Take Home Message

Conclusions:

- The Genomic Health Clinical Laboratory Experience with the GPS test confirms a wide spectrum of individual tumor biology within traditional clinical risk groups.
- Over 1 in 3 men had a post-GPS risk assignment different from the submitted NCCN risk group.
- Patients in NCCN Low and Intermediate risk groups were more frequently reclassified upon GPS testing than the NCCN Very Low risk group.
- Use of GPS testing provides physicians and patients with personalized information to improve risk assessment and guide better decision making for initial disease management.
- While it is always important to understand which patients harbor more aggressive disease, during the COVID-19 pandemic the GPS test enables physicians to confidently prioritize and treat men who are at higher risk once it is deemed safe to do so.

Plain Language Summary: In this study, we compared the NCCN risk group that was assigned upon ordering of the GPS test to the classification that resulted after GPS testing, from the Genomic Health Commercial database. We found that over 1 in 3 men had a change in risk assignment upon GPS testing. Use of the GPS test may provide physicians and patients with personalized information of risk assessment and guide decision making for prostate cancer management.

RESULTS

Table 1. Risk Group Refinement Comparing Submitted NCCN Risk Group with Post-GPS Risk Group

Submitted NCCN Risk Group	Post-GPS Risk Group: VL Risk n (%)	Low Risk n (%)	FIR n (%)	IR[1,2] n (%)	High Risk n (%)	Difference: Lower	Same	Higher
Very Low Risk n = 6,230 (19%)	5,787 (93%)	356 (6%)	70 (1%)	5 (< 1%)	12 (< 1%)	0 (0%)	5,787 (93%)	443 (7%)
Low Risk n = 12,839 (40%)	5,570 (43%)	4,887 (38%)	1,994 (16%)	329 (3%)	59 (< 1%)	5,570 (43%)	4,887 (38%)	2,382 (19%)
Intermediate Risk n = 13,361 (41%)	0 (0%)	2,115 (16%)	1,011 (8%)	7,807 (58%)	2,428 (18%)	2,115 (16%)	8,818 (66%)	2,428 (18%)

[1] "Unfavorable Intermediate" was changed to "Intermediate" in Feb 2019

[2] Patients with submitted NCCN Intermediate Risk confirmed to have FIR following GPS testing may potentially be eligible for active surveillance. Further retrospective studies are underway to confirm rates of receiving active surveillance in this subgroup.

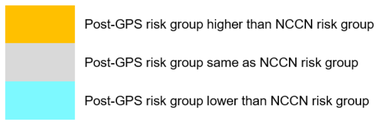
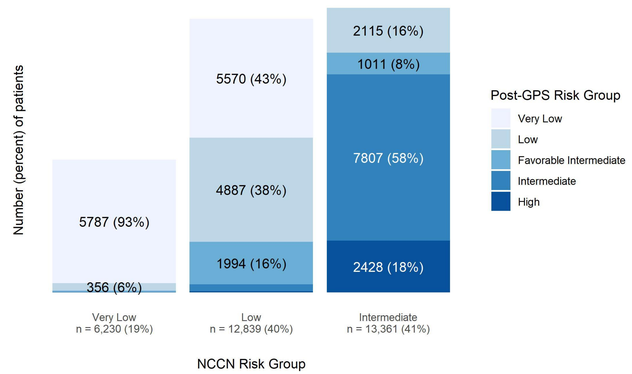


Figure 2. GPS Risk Group Refinement Compared to Submitted NCCN Risk Group



RESULTS

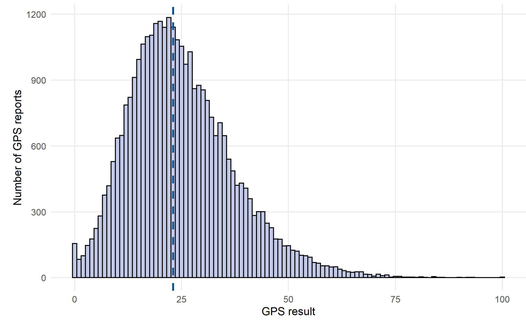
Table 2. Clinical/Pathological Characteristics by Submitted NCCN Group

	Overall (n = 32,430)	Submitted NCCN Risk Group: Very Low (n = 6,230)	Low (n = 12,839)	Intermediate (n = 13,361)
Patient age				
Median (IQR)	66 (60, 71)	65 (60, 70)	65 (59, 69)	67 (62, 72)
Range	35, > 89	36, > 89	35, 88	40, > 89
< 65	13,942 (43%)	2,903 (47%)	6,318 (49%)	4,721 (35%)
≥ 65	18,473 (57%)	3,323 (53%)	6,517 (51%)	8,633 (65%)
Missing	15 (< 1%)	4 (< 1%)	4 (< 1%)	7 (< 1%)
Gleason Score				
3+3	21963 (68%)	6,230 (100%)	12,839 (100%)	2,894 (22%)
3+4	9748 (30%)	0	0	9,748 (73%)
4+3	719 (2%)	0	0	719 (5%)
PSA (ng/mL)				
Median (IQR)	5.7 (4.5, 7.6)	4.9 (4.0, 6.0)	5.5 (4.5, 7.0)	6.6 (4.8, 10.0)
Clinical Stage				
T1c	28,443 (88%)	6,230 (100%)	11,284 (88%)	10,929 (82%)
T2a	2767 (9%)	0	1,554 (12%)	1,213 (9%)
T2b	581 (2%)	0	0	581 (4%)
T2c	639 (2%)	0	1 (0.01%)[1]	638 (5%)
Percent positive cores				
Median (IQR)	17% (8%, 33%)	8% (8%, 17%)	25% (15%, 33%)	25% (15%, 38%)
Number missing	1,088	175	346	567
GPS				
Median (IQR)	23 (16, 32)	20 (14, 27)	21 (15, 29)	28 (20, 37)

Footnotes:

[1]One patient submitted as Low Risk, but has GS 3+3, PSA = 5.8 ng/mL, clinical stage T2c. According to NCCN guidelines, this patient should be classified as intermediate.

Figure 3. Histogram of GPS Results for 32,430 Assays



- Histogram bins are one GPS unit each.
- Dashed line is the median GPS result (23).

REFERENCES

1. Moschini et al. *BMC Medicine.* 2016.
2. Klein et al. *Eur Urol.* 2014.

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