New genetic assays to help prostate cancer patients avoid radiation toxicity

PROSTOX®

MiraDx's PROSTOX assays analyze germline DNA to determine if a patient has a genetically higher risk of late grade ≥ 2 genitourinary (GU) toxicity following radiation therapy (RT).

Two PROSTOX tests provide a Low-Average Risk or High Risk result to help choose the safest course of treatment to avoid toxicity in the management of a patient's PC. If a patient is High Risk on one test, there is only a 10% chance that they will be High Risk on the other test, supporting that very few patients (~1-2%) are "radiosensitive" (defined as High Risk on both tests) and should consider other options for the treatment of their PC.

PROSTATE CANCER (PC) OVERVIEW

PC affects nearly 334,000 patients each year and is the second leading cause of cancer mortality in men in the U.S.[1] It mainly affects those over 65 years of age. If the cancer is localized, there is an excellent five-year survival rate of > 99%.[2]

TREATMENT OPTIONS AND SIDE EFFECTS

Physicians and patients often face difficult choices when deciding on a course of treatment for PC. Among those who opt for definitive therapy, nearly half receive radiation treatment.[3]

However, 15-20% or more of patients treated with RT develop late grade ≥ 2 genitourinary (GU) toxicity. This can include urinary retention, pain, increased urinary frequency, and bleeding.[4,5] Rates of late GU toxicity are slightly higher when patients are treated with SBRT (> 7 Gy per fraction over 7 or fewer sessions) compared to treatment by MHFRT or CFRT (1.8–3 Gy per fraction over 20-35 or more sessions).[6,7]

mirSNP DNA SIGNATURES AND RADIATION TOXICITY

Genomic factors influence clinical radiosensitivity. miRNAs are small, non-coding RNAs that regulate stress responses, including DNA damage and immune pathways, and are critical in radiation therapy responses.[8,9] Alterations in miRNA circuitry through single nucleotide polymorphisms (mirSNPs) can affect treatment outcomes. Unique mirSNP DNA signatures—such as those analyzed by the PROSTOX tests—can help predict individual radiosensitivity risk.

THE PROSTOX ASSAYS

PROSTOX Ultra

Predicts toxicity from stereotactic body radiotherapy (SBRT)[10]

96%	70%	95%	77%*
NPV	Sensitivity	Specificity	PPV

PROSTOX Standard

Predicts toxicity from conventionally fractionated radiotherapy (CFRT) and moderately hypofractionated radiotherapy (MHFRT).[10,11]

93%	70%	95%	75%*
NPV	Sensitivity	Specificity	PPV

Tests are convenient, non-invasive DNA tests, consisting of germline DNA collected and analyzed from buccal swabs.

*Data based on patients from clinical trials and real-world clinical settings. (see refs. 10, 12, and 13 for PROSTOX *Ultra*; refs. 10 and 11 for PROSTOX *Standard).*

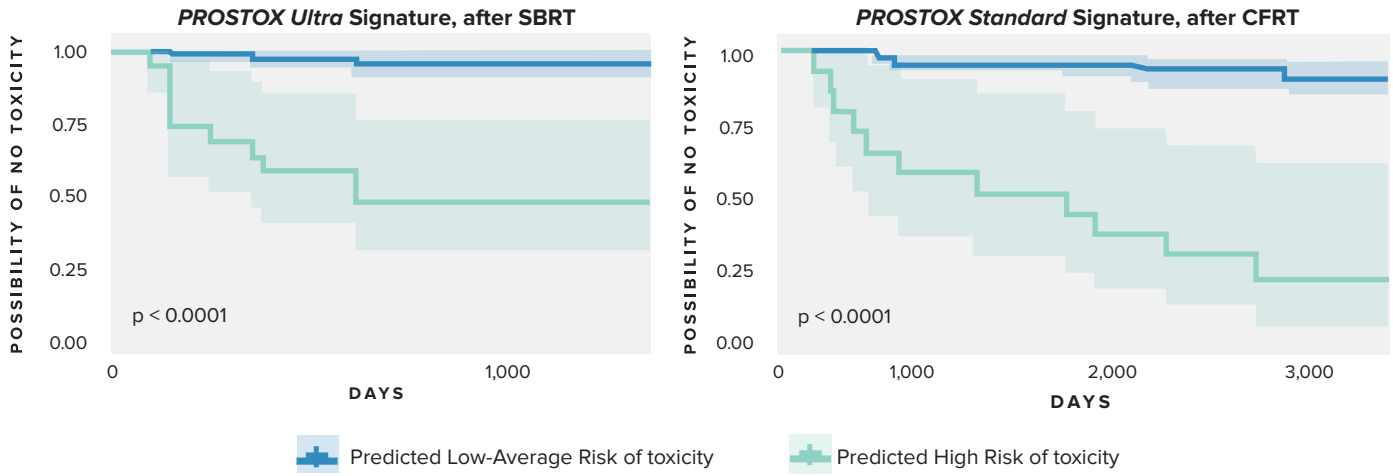
NEW CLASS OF GENETIC VARIANTS APPLIED

Certain miRNA-associated germline variants (mirSNPs) influence the risk of late GU toxicity to RT; in 2022, researchers identified specific mirSNP signatures that predict late grade ≥ 2 GU toxicity following either SBRT or CFRT.[10]

These findings have been validated in multiple contexts, including in the post-op SBRT setting and in a clinical utility study.[12,14] An independent validation study confirmed that the signatures reliably identify patients at increased risk of late GU toxicity from both CT- and MRI-guided SBRT.[13] A prospective registry study further demonstrated that the PROSTOX Standard signature predicts risk of toxicity in patients receiving MHFRT.[11]

Together, these results offer a practical tool to guide the selection of the safest RT approach for individual patients, helping to avoid late radiation toxicity.

Performance of predictive model for late grade ≥ 2 genitourinary toxicity[10]



	CLINICAL UTILITY	RANGE	METHOD	SPECIMEN TYPE/COLLECTION
PROSTOX Ultra* and *PROSTOX Standard	Analysis of germline DNA to identify genetic variants that predict increased risk of late grade ≥ 2 GU toxicity following RT	Low-Average Risk High Risk	Predictive algorithm utilizing PCR- or mass spectrometry-based genotyping	Buccal mucosal cells collected with a swab and test kit and returned to MiraDx Laboratory

Note: The PROSTOX tests are currently not validated in patients undergoing brachytherapy.

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