New genetic assays to help prostate cancer patients avoid radiation toxicity

PROSTOX™

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MiraDX's **PROS**TOX 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 **PROS**TOX tests provide a low or high risk result to help choose the safest course of treatment to avoid toxicity in the management of a patient's prostate cancer (PC). If a patient is high risk to one test, there is only a 10% chance that they will be high risk to the other test, supporting that very few patients (~1%) are "radiosensitive" and unable to receive RT for the treatment of their PC.

PROSTATE CANCER OVERVIEW

PC affects nearly 270,000 patients each year,[1] and is the third leading cause of cancer mortality in men[2] in the U.S. It mainly affects those over 65 years of age. If the cancer is localized, there is an excellent five-year survival rate of >99%.[1]

TREATMENT OPTIONS AND SIDE EFFECTS

Physicians often face difficult choices when deciding on a course of treatment for PC patients. RT is an effective treatment option and is performed on approximately half of men diagnosed with localized PC.

However, 15% or more of patients treated with RT develop late grade ≥2 GU toxicity. This can include urinary retention, pain, increased urinary frequency, and bleeding.[3,4] Rates of late GU toxicity are similar whether treatment is delivered by CFRT (1.8-2.0 Gy per fraction over 35 or more sessions) or SBRT (>7 Gy per fraction over 7 or less sessions).[5,6]

mirSNP DNA SIGNATURES AND RADIATION TOXICITY

Genomic factors play an important role in clinical radiosensitivity. miRNAs are small, non-coding regulatory RNAs that are key directors of stress response pathways, including the DNA damage and immune responses. miRNAs have also been found to be critical in the response to RT, both locally and systemically.[7]

THE PROSTOX ASSAYS*

PROSTOX *ultra*

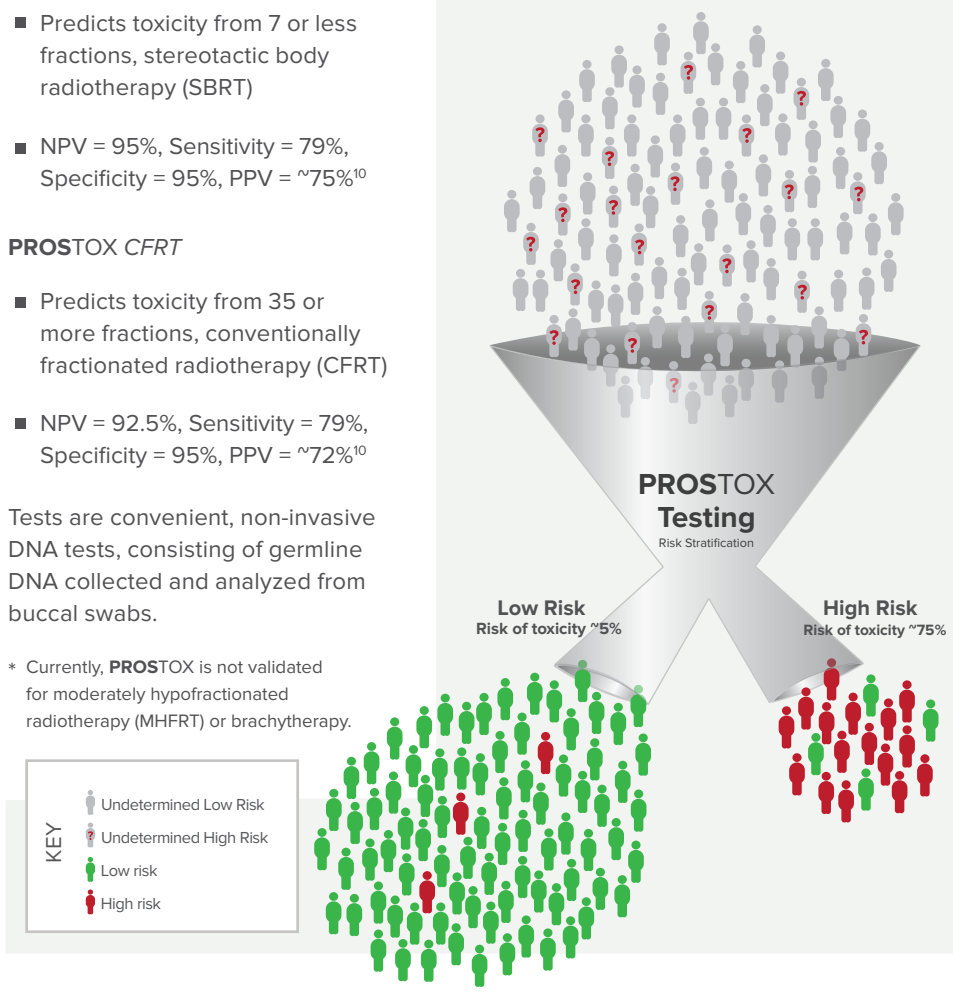
- Predicts toxicity from 7 or less fractions, stereotactic body radiotherapy (SBRT)
- NPV = 95%, Sensitivity = 79%, Specificity = 95%, PPV = ~75%[10]

PROSTOX *CFRT*

- Predicts toxicity from 35 or more fractions, conventionally fractionated radiotherapy (CFRT)
- NPV = 92.5%, Sensitivity = 79%, Specificity = 95%, PPV = ~72%[10]

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

* Currently, **PROS**TOX is not validated for moderately hypofractionated radiotherapy (MHFRT) or brachytherapy.

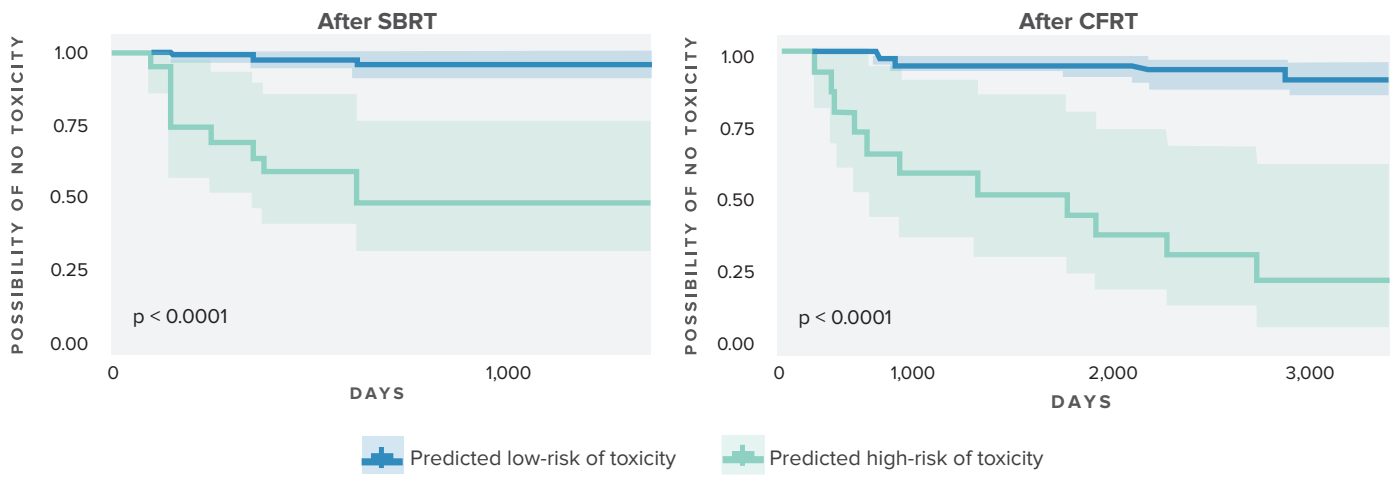


NEW CLASS OF GENETIC VARIANTS APPLIED

Recent studies have identified miRNA-associated germline single nucleotide polymorphisms (mirSNPs) that play a key role in determining a patient's risk of late GU toxicity to RT.[8,9]

A 2022 study identified mirSNP signatures that predict late grade ≥2 GU toxicity following SBRT or CFRT.[10] These findings have now been independently validated in a post-op SBRT study[11] as well as in a clinical utility study.[12] **These signatures allow the safest RT approach to be selected to help avoid late radiation toxicity.**

Performance of predictive model for late grade ≥2 genitourinary toxicity



PROSTOX ORDERING INFORMATION

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

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