New genetic assays to help prostate cancer patients avoid radiation toxicity

PROSTOX™

PROSTATE CANCER OVERVIEW

Prostate cancer (PC) affects nearly 270,000 patients each year,[1] and is the third leading cause of cancer mortality in men2 in the U.S. PC 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 prostate cancer patients. Radiation therapy (RT) can be an effective treatment option and is performed on approximately half of men diagnosed with localized prostate cancer. However, about 12-15+% of these men experience late grade >2 genitourinary (GU) toxicity, which can result in urinary retention, pain, increased urinary frequency, and bleeding.[3,4] Rates of late GU toxicity can occur whether treated by conventionally fractionated radiotherapy (CFRT; 1.8-2.0 Gy per fraction over 35-45 sessions) or stereotactic body radiotherapy (SBRT; >7 Gy per fraction over 4-7 sessions).[5,6]

MIRSNP DNA SIGNATURES AND RADIATION TOXICITY

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

PROSTOX

MiraDX's **PROS**TOX assays analyze germline DNA to determine if a patient has a genetically higher risk of late grade ≥2 genitourinary toxicity following radiation therapy.

The **PROS**TOX tests provide a low or high risk score to help identify the safest course of treatment to avoid toxicity in the management of a patient's prostate cancer.

THE PROSTOX ASSAYS

PROSTOX *ultra*

Predicts late grade 2 or higher GU toxicity after prostate directed stereotactic body radiation therapy (SBRT):

NPV = 95%, Sensitivity = 79%, Specificity = 95%, PPV = ~75% [10]

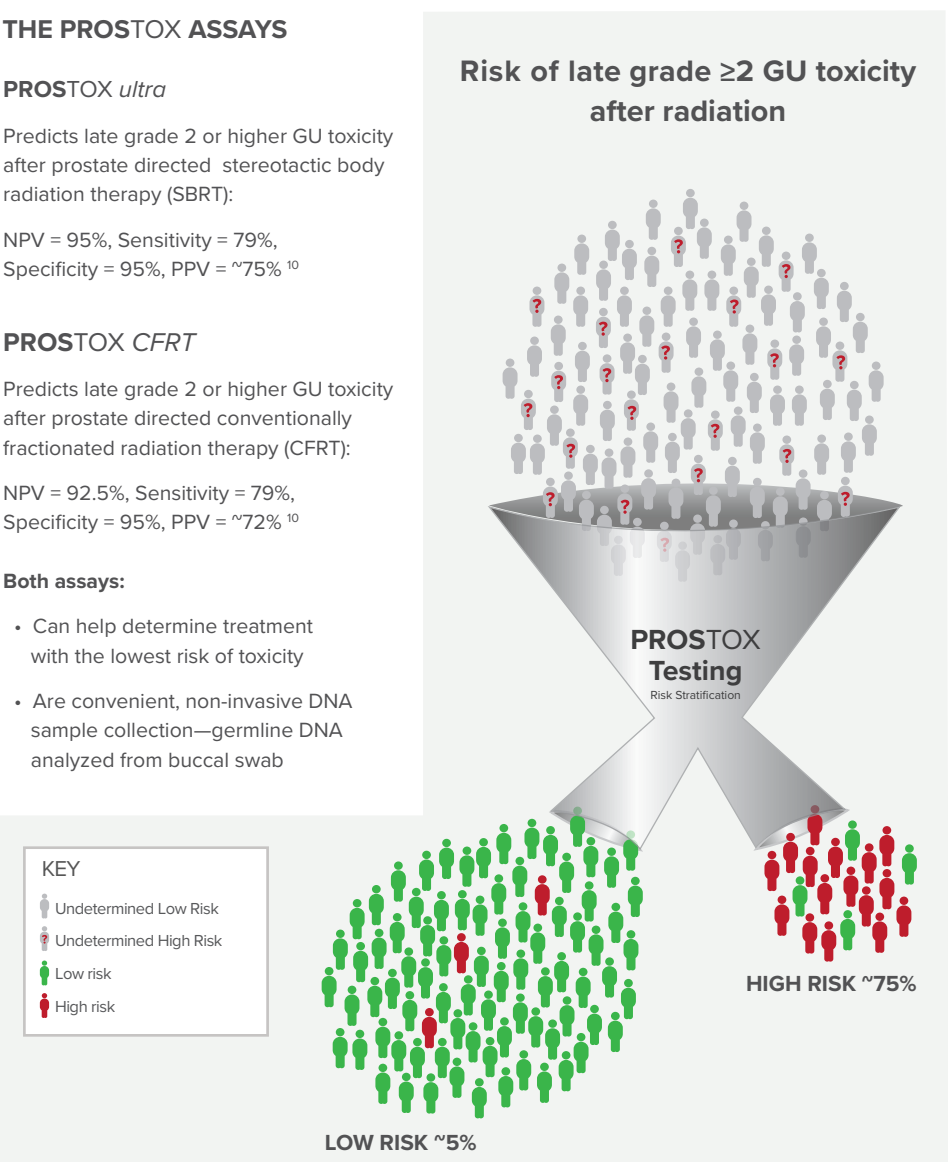
PROSTOX *CFRT*

Predicts late grade 2 or higher GU toxicity after prostate directed conventionally fractionated radiation therapy (CFRT):

NPV = 92.5%, Sensitivity = 79%, Specificity = 95%, PPV = ~72% [10]

Both assays:

- Can help determine treatment with the lowest risk of toxicity
- Are convenient, non-invasive DNA sample collection—germline DNA analyzed from buccal swab

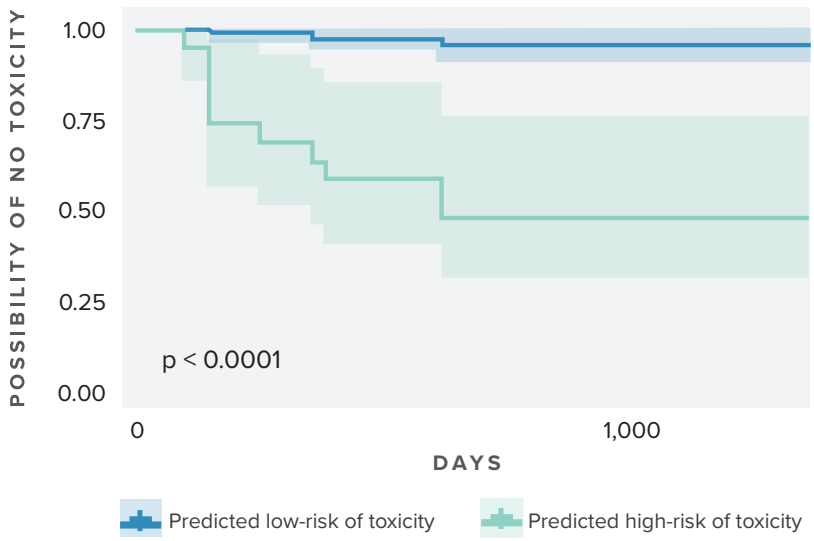


NEW CLASS OF GENETIC VARIANTS APPLIED

Recent studies have identified miRNA associated germline single nucleotide polymorphisms (mirSNPs) that appear to play a key role in determining a patient's response to radiation therapy.[8,9]

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

Performance of predictive model for late grade ≥2 genitourinary toxicity after conventionally-fractionated radiotherapy or SBRT.



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 radiation therapy.	Low risk High risk	Predictive algorithm utilizing PCR-based Taqman genotypin	Oral mucosal cells collected with a swab and test kit and returned to MiraDX Laboratory

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