Clinical significance of the Siaα2,3Gal-glycosylated Prostate-Specific Antigen Assay for prostate cancer detection

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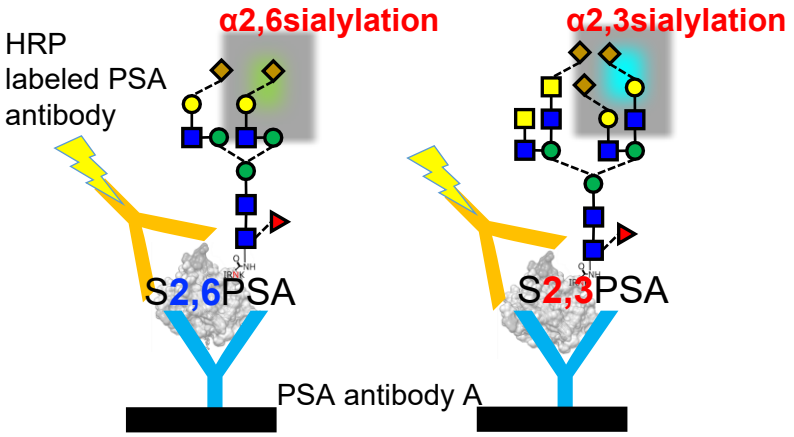
Conflict of Interest Disclosure

I have no potential conflict of interest to report

Background & Objective:

PSA test VS

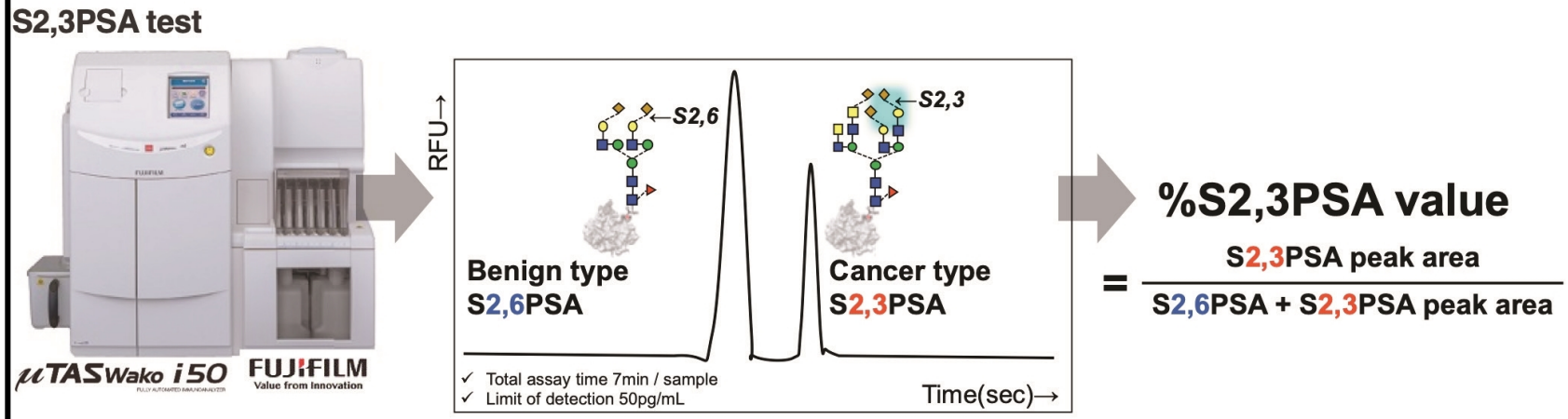
Quantitative analysis of PSA in serum
(prostate specific, but **not PC specific**)



S2,3PSA test

microfluidic capillary electrophoresis-based immunoassay system

Ratio of PC specific glycan change of PSA in serum (**PC specific**)



To reduce unnecessary prostate biopsies, better discrimination is needed.
We previously established a microfluidic capillary electrophoresis-based immunoassay system to detect PC-associated terminal Siaα2,3Gal-glycosylated prostate-specific antigen in serum[1, 2].

Ref1.Yoneyama et al. ***BBRC*, 448:** 390, 2014 Ref 2.Ishikawa et al. ***Int .J. Mol. Sci.*, 18**, E470, 2017

Background & Objective:

Training cohort study

Between 2008-2017 TRUS-guided Prostate biopsy (*n*=554) performed in **four institutes.**
Hirosaki, Tohoku & Akita University in Japan
McMaster University in Canada.

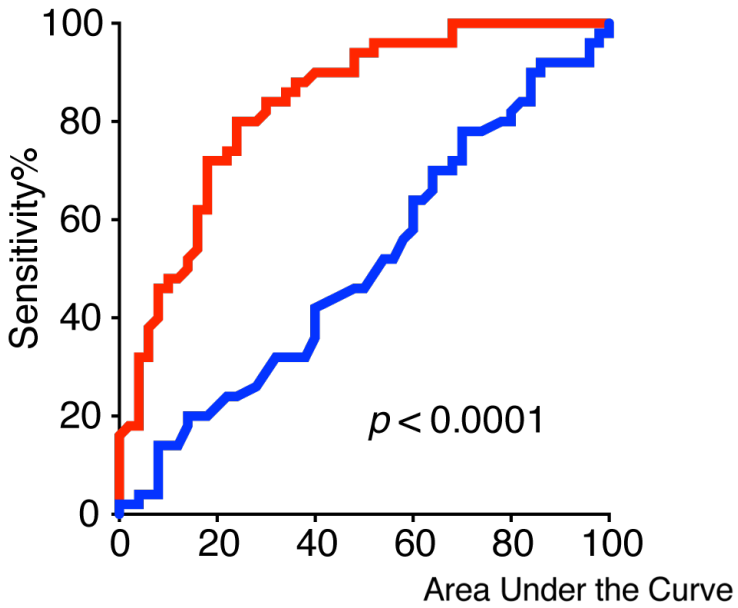
Serum available sample (less than PSA 20 ng/mL)

Age & PSA level matching

Biopsy-proven BPH
***n* = 50**

Determine cutoff value and diagnostic performance was compared between %S2,3PSA & total PSA

Biopsy-proven PCa
***n* = 50**

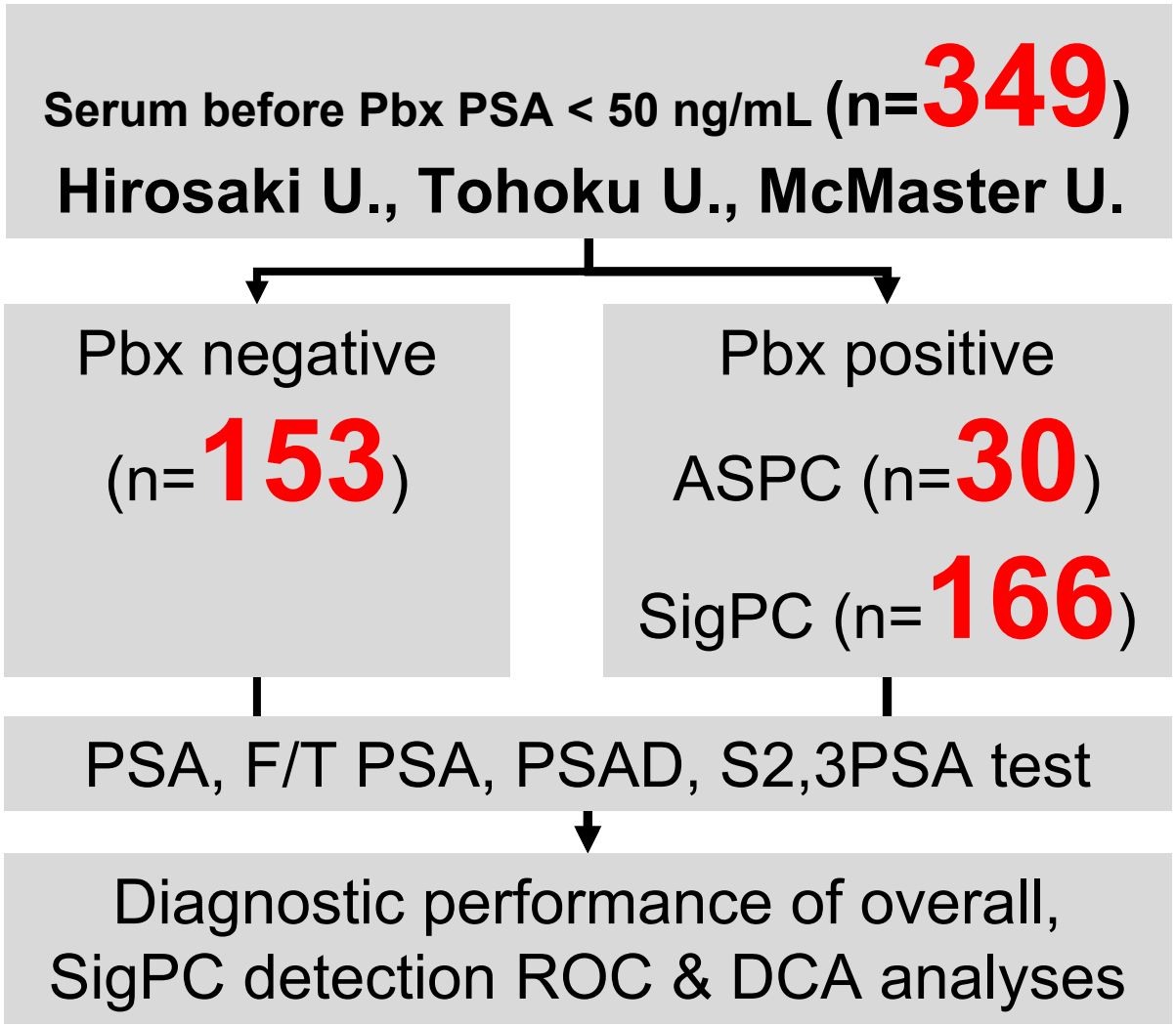


%S2,3PSA test may improve the accuracy of prostate cancer diagnosis in clinical setting.

The aim of this study to compare the diagnostic performance between S2,3PSA test and PSA based testing in validation cohort.

Ishikawa et al. ***Int .J. Mol. Sci.***, **18**, E470, 2017

Design, Setting, and participants of Pbx cohort:

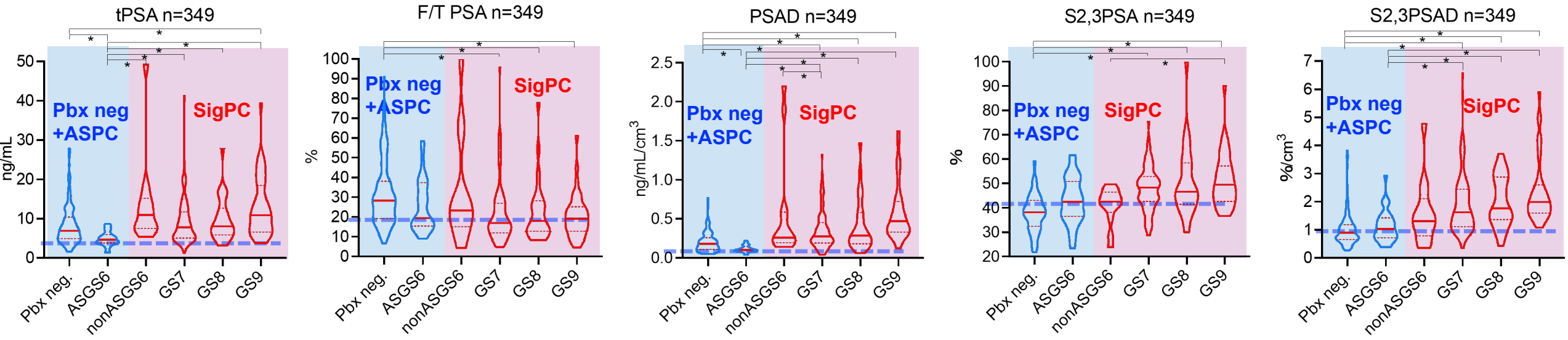


Biopsy outcome	negative[a]	ASPC[b]	SigPC[c]		p Value	
All (n = 349)	(n = 152)	(n = 30)	(n = 166)	a vs b	a vs c	b vs c
Median age (IQR)	67 (62.0–74.0)	66.5 (63.0–73.3)	67 (63.0–73.0)	0.992	0.509	0.701
DRE status normal/abnormal	138/14	24/6	105/61	0.041	<0.0001	0.167
Median P vol cm^3 (IQR)	42.8 (30.3–55.8)	42.8 (33.5–50.0)	26.3 (20.1–36.1)	0.781	<0.0001	<0.0001
Median tPSA ng/mL (IQR)	6.90 (4.85–10.30)	4.63 (3.80–5.93)	8.36 (5.78–13.11)	<0.0001	<0.0001	<0.0001
Median F/T PSA % (IQR)	28.3 (19.3–38.1)	19.5 (15.4–37.4)	18.3 (12.6–26.8)	0.042	<0.0001	<0.0001
Median PSAD ng/mL/cm3 (IQR)	0.17 (0.10–0.25)	0.11 (0.09–0.16)	0.36 (0.22–0.66)	<0.0001	<0.0001	<0.0001
Median S2,3PSA % (IQR)	38.3 (32.4–43.0)	42.4 (36.5–50.9)	47.3 (42.0–53.9)	0.003	<0.0001	0.003
Median S2,3PSAD %/cm3 (IQR)	0.91 (0.67–1.20)	1.03 (0.72–1.42)	1.76 (1.27–2.49)	0.208	<0.0001	<0.0001
Clinical T stage		n (%)	n (%)			
1c		24 (80)	95 (57.2)			
2a		5 (26.6)	27 (16.3)			
2b		1 (3.3)	15 (9.0)			
2c-3		0 (0)	29 (17.4)			
prostate biopsy GS sum		n (%)	n (%)			
GS 6		30 (100)	14 (8.4)			
GS 7		0 (0)	87 (52.4)			
GS 8		0 (0)	26 (15.7)			
GS 9		0 (0)	39 (23.5)			

ASPC: Active surveillance eligible PC by PRIAS criteria
SigPC: non-ASPC

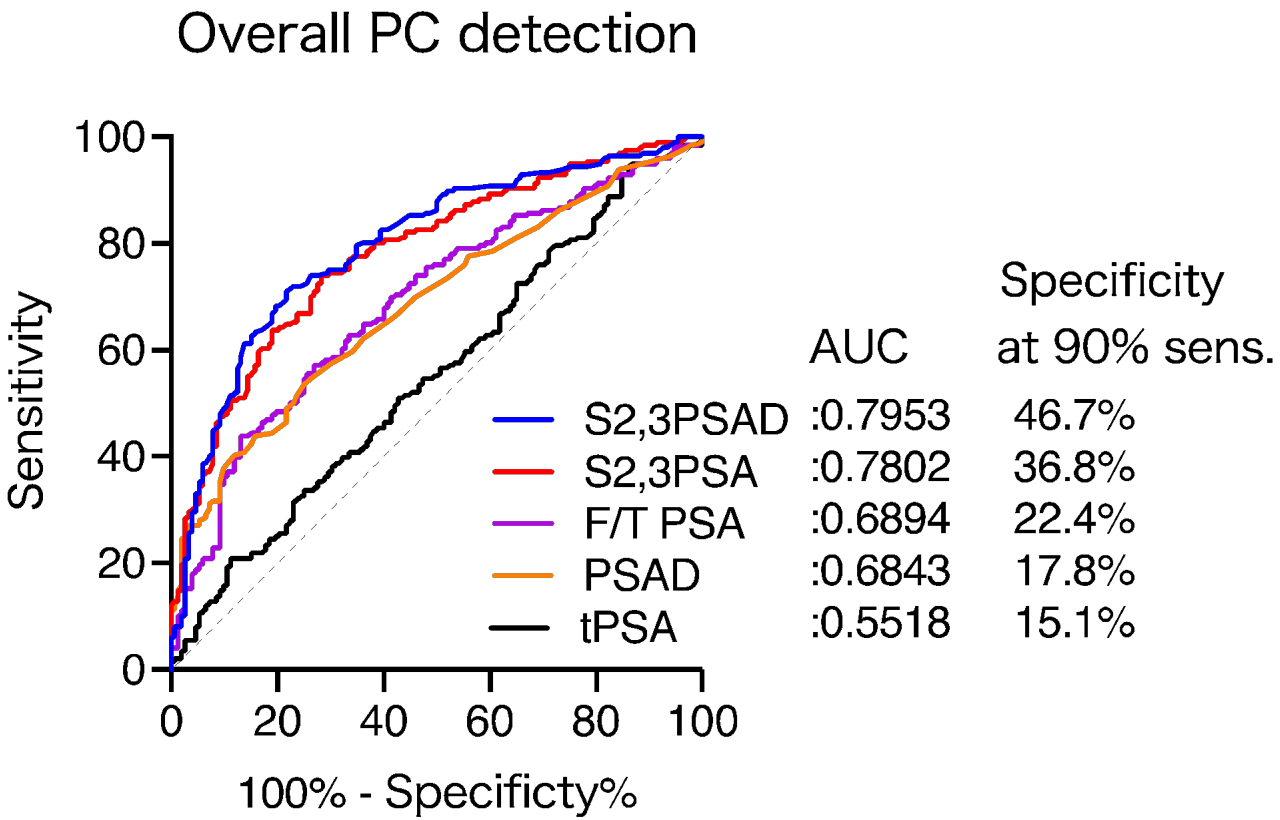
The assays were retrospectively evaluated using the AUC of ROC analysis and DCA analysis to discriminate overall PC, SigPC

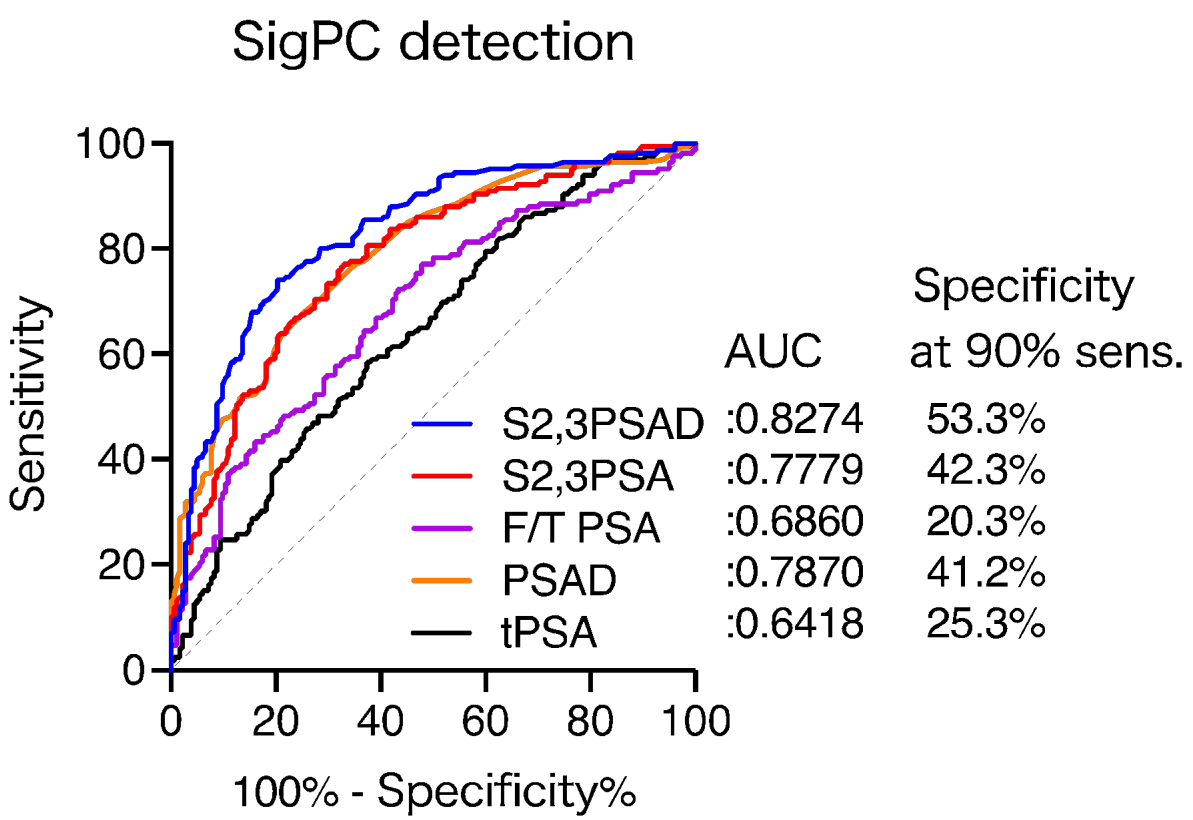
Violin plot in Pbx cohort



- **Serum level of S2,3PSA** was **increased in overall PC.**
- **Serum level of S2,3PSAD** was **significantly increased in SigPC.**

ROC analysis in Pbx cohort





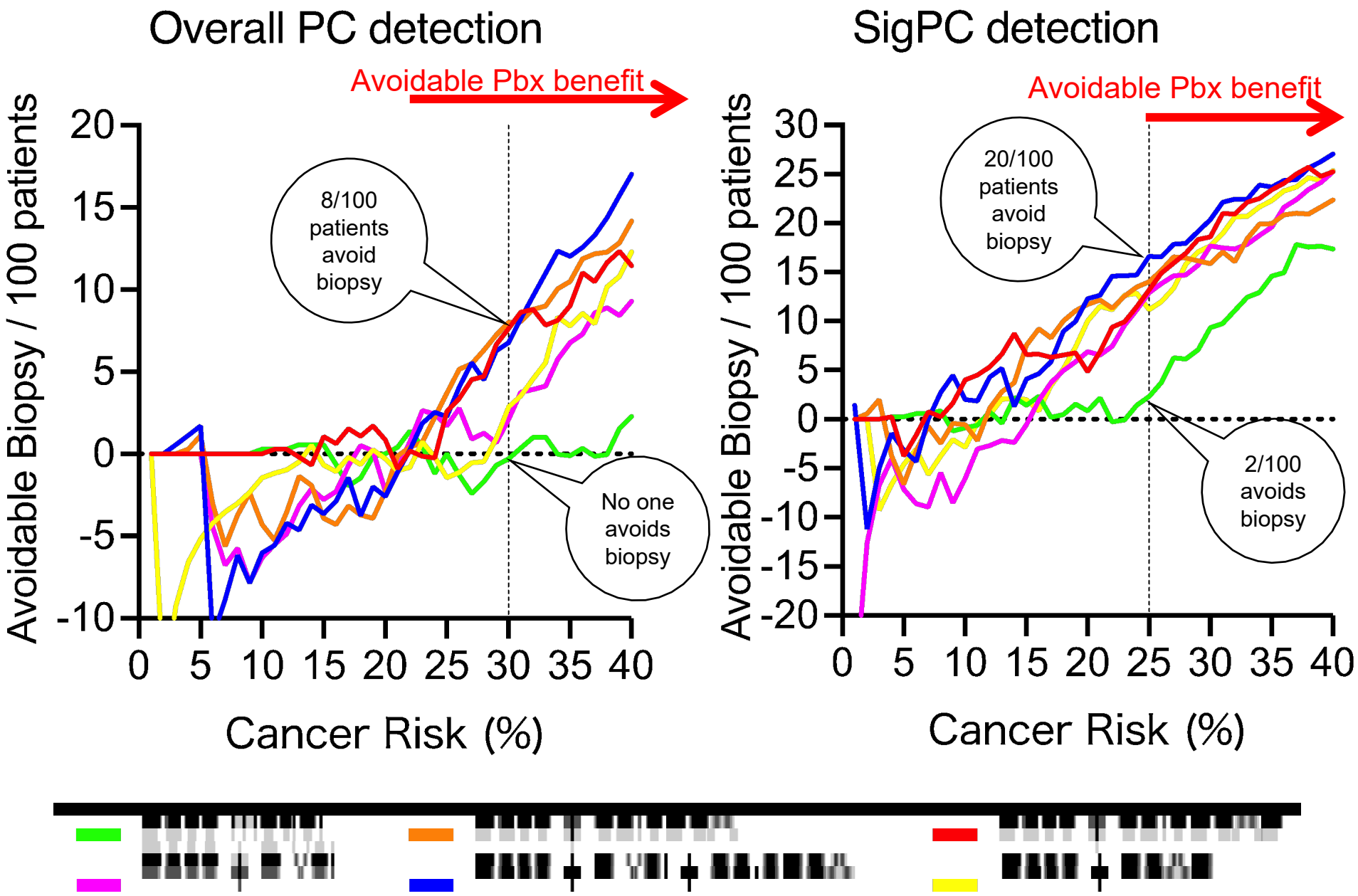
➢**S2,3PSAD had the largest AUC (0.7953 for overall PC) (0.8274 for SigPC)** and provided significantly better clinical performance for discriminating overall PC & SigPC compared with conventional test.

NPV, PPV & Specificity @ 90 sensitivity in Pbx cohort

Overall PC detection	tPSA	F/T PSA	PSAD	S2,3PSA	S2,3PSAD
Cut-off	4.38 ng/mL	41.90%	0.095 ng/mL/cm3	35.90%	0.825 %/cm^3
AUC; p (vs LDN-PSAD)	0.5518 ; p <0.0001	0.6894 ; p <0.0001	0.6843 ; p <0.0001	0.7802 ; p = 0.0026	0.7953
PPV, %	57.1	59.4	58.1	**63.9**	**67.7**
NPV, %	53.8	64.8	61.4	**73.7**	**78.0**
Specificity, %	18.4	23.0	17.8	**36.8**	**46.7**
SigPC detection	tPSA	F/T PSA	PSAD	S2,3PSA	S2,3PSAD
Cut-off	4.58 ng/mL	41.90%	0.135 ng/mL/cm3	37.20%	0.975 %/cm^3
AUC; p (vs LDN-PSAD)	0.6418 ; p <0.0001	0.6860 ; p <0.0001	0.7870 ; p <0.0001	0.7779 ; p = 0.0026	0.8247
PPV, %	52.3	51.0	58.4	**59.3**	**65.0**
NPV, %	72.1	68.5	82.8	**81.9**	**84.0**
Specificity, %	24.7	20.8	40.4	**43.3**	**56.2**

- **S2,3PSA(D)** provided significantly better **NPV and PPV** for discriminating overall PC & SigPC compared with conventional test.

Decision curve analysis in Pbx cohort



Decision curve analysis in Pbx cohort

	Risk threshold (%) of overall cohort					
Pbx avoided per 100 patients w/o missing overall PC	10	15	20	25	30	35
Base model	0.3	0.6	0.0	0.0	-0.3	-0.1
Base+ P vol.	-6.3	-2.8	-2.3	1.7	2.1	6.8
Base+ PSAD	-1.4	-0.7	-0.3	-1.4	2.9	7.8
Base+ S2,3PSA	-4.3	-3.9	-2.3	**3.7**	**8.0**	**10.5**
Base+ P vol.+ S2,3PSA	-6.0	-3.6	-2.6	**2.3**	**6.8**	**12.0**
Base+ S2,3PSAD	0.0	1.1	0.9	**2.6**	**7.6**	**9.0**
Pbx avoided per 100 patients w/o missing SigPC	10	15	20	25	30	35
Base model	-0.9	1.4	0.9	2.3	9.4	14.6
Base+ P vol.	-6.0	-0.6	6.9	12.9	17.7	19.6
Base+ PSAD	-0.6	7.5	11.7	14.0	15.9	19.9
Base+ S2,3PSA	2.0	4.1	12.3	**16.6**	**20.3**	**23.7**
Base+ P vol.+ S2,3PSA	4.0	6.6	4.9	**13.2**	**18.6**	**23.4**
Base+ S2,3PSAD	-2.9	2.0	10.0	**11.2**	**17.7**	**22.3**

- **Base (age, DRE, tPSA, F/T) + S2,3PSA** is the best option ≥ 25 % risk threshold.
- **Adding S2,3PSA & S2,3PSAD** to the base model permitted avoidance of even more biopsies w/o missing overall & SigPC.

Conclusion:

- **The diagnostic performance of S2,3PSA(D)** is **significantly better than the PSA, FT/ PSA & PSAD test** in identifying patients with overall PC and SigPC.

- **Addition of S2,3PSA** test to conventional diagnostic model **significantly improve avoidable biopsy effect** in identifying patients with overall PC and sigPC.