

SMARTER USE OF ROUTINELY COLLECTED DATA: THE VALUE OF PSA DYNAMICS FOR PROSTATE CANCER RISK STRATIFICATION

Jane Shortall, Eliana Vasquez Osorio, Andrew Green, David Wong, Tanuj Puri, Peter Hoskin, Ananya Choudhury, Marcel van Herk and Alan McWilliam

The University of Manchester



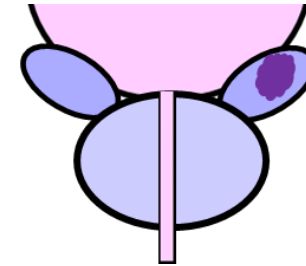
PROSTATE CANCER

52,000 diagnosed /year
17,000 radiotherapy / year



1 in 3 recur¹

Voxel-Based Analysis (VBA):
Lower dose in seminal vesicles → BCR

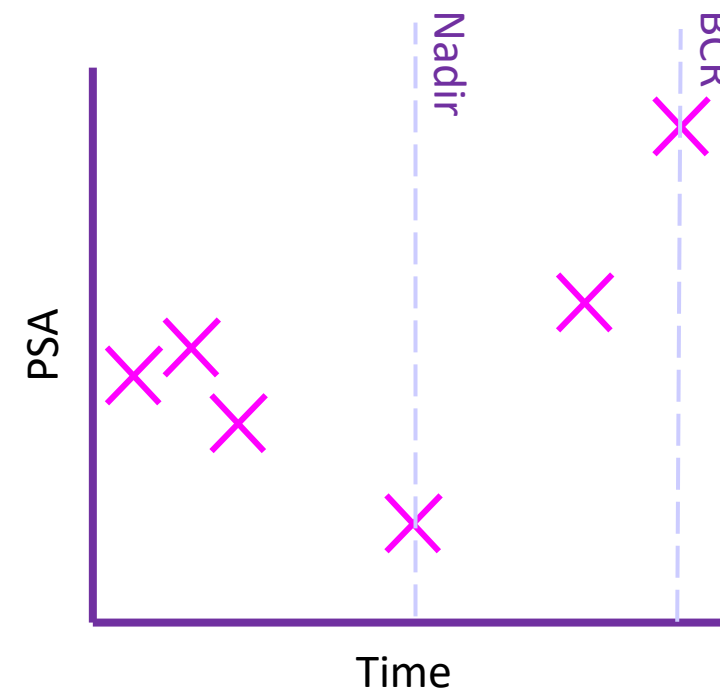


Under-treated seminal vesicle invasion²

DETECTING RECURRENCE

Prostate Specific Antigen (PSA): nadir + 2ng/ml¹

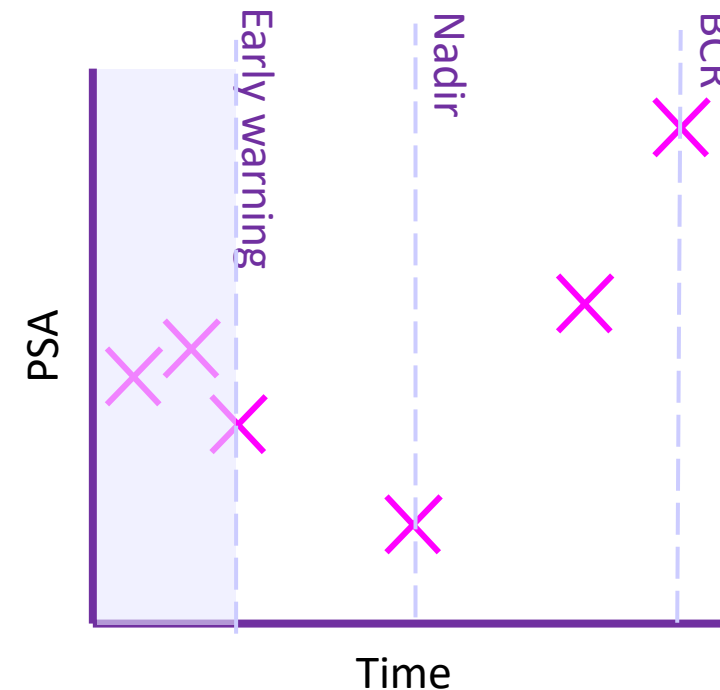
- × Patient defined threshold
- × Detected after event
- × PSA measurements sporadic and irregular
- × Opportunity for early intervention often missed



DETECTING RECURRENCE: BETTER

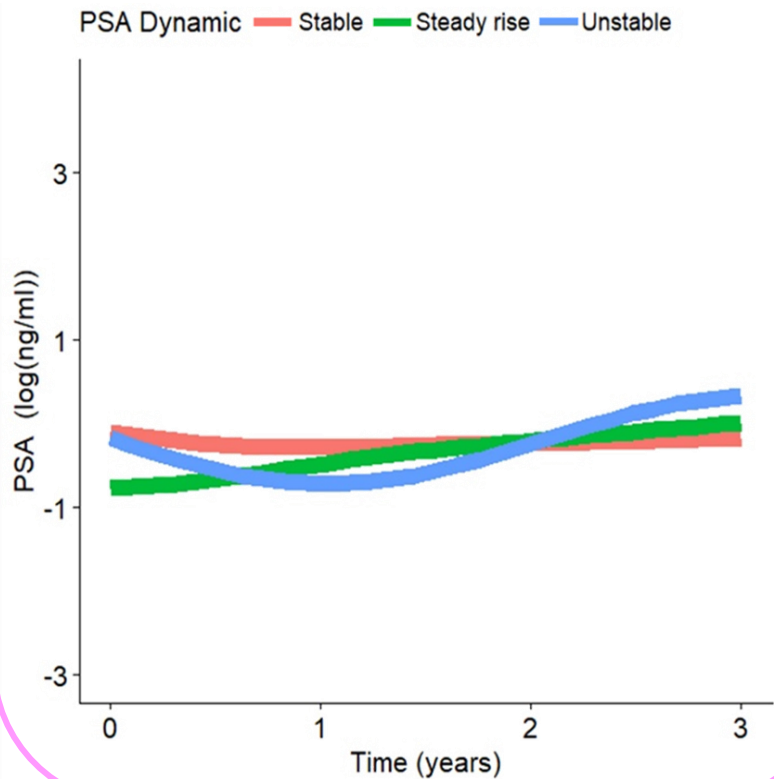
Can short-term post-radiotherapy PSA dynamics predict long term outcome?

- ✓ Re-stratify BCR risk after radiotherapy
- ✓ More appropriate follow-up
- ✓ Intervene with salvage treatment quicker
- ✓ Reassure some patients

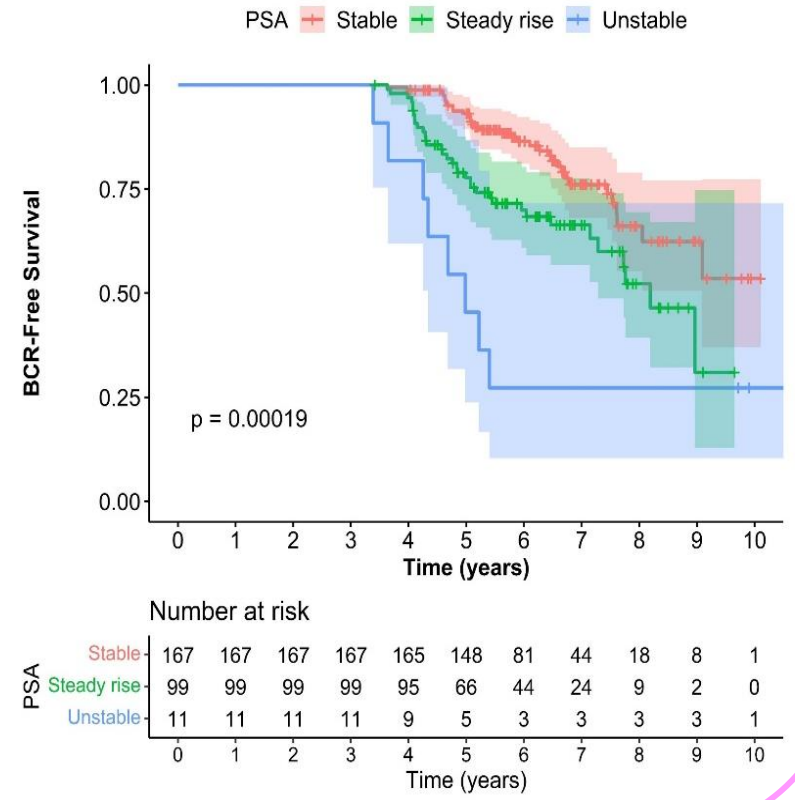
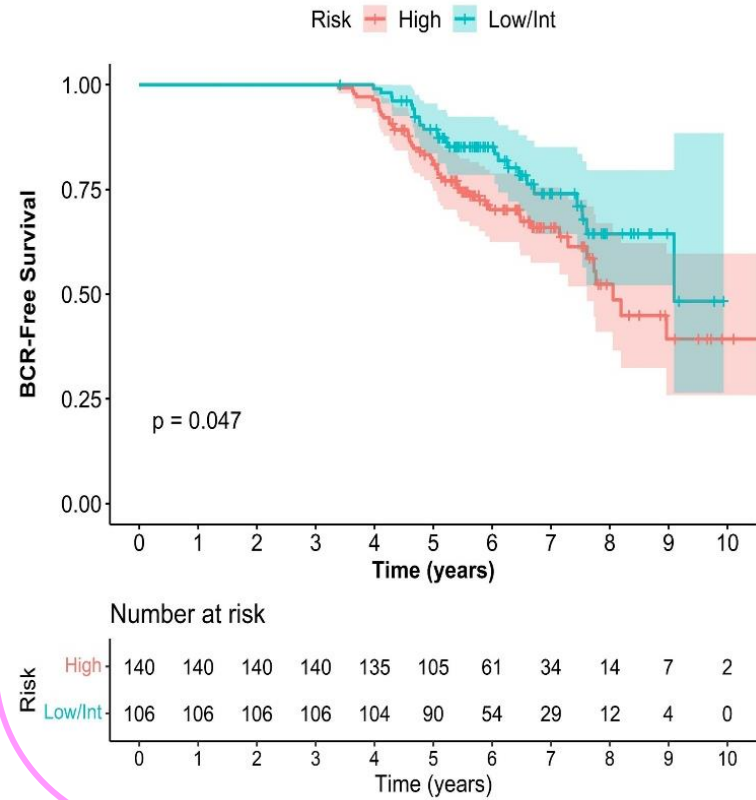


EARLY PSA DYNAMICS PREDICT LATER BCR

Characteristic PSA dynamics
First 3-years of follow-up
Manchester hypo-fractionated (n=277)

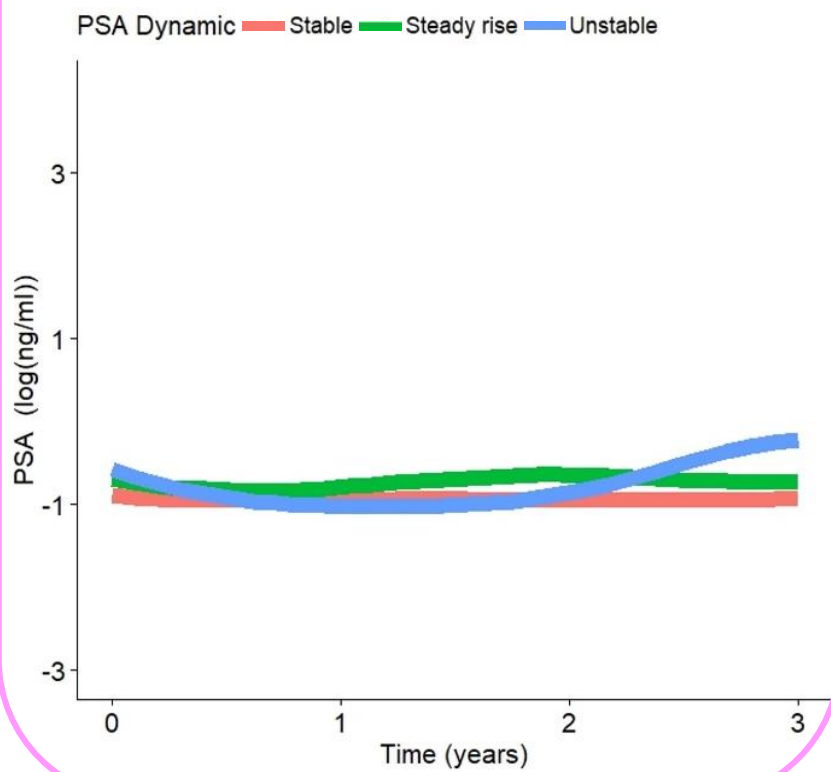


More prognostic than pre-treatment risk
Post radiotherapy re-stratification

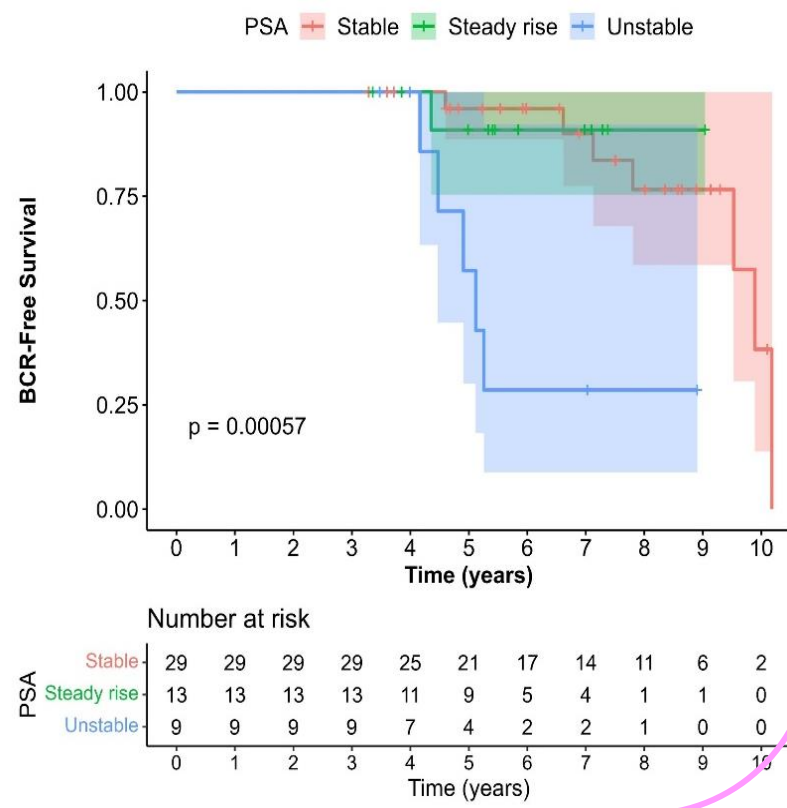
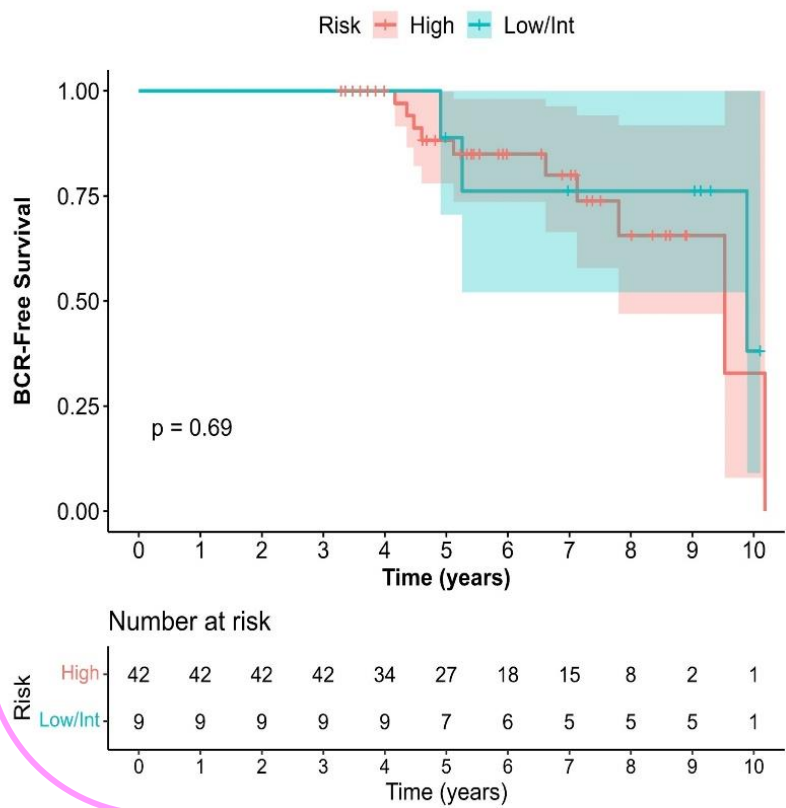


EARLY PSA DYNAMICS PREDICT LATER BCR

Characteristic PSA dynamics
First 3-years of follow-up
Manchester brachytherapy* (n=51)



More prognostic than pre-treatment risk
Post radiotherapy re-stratification

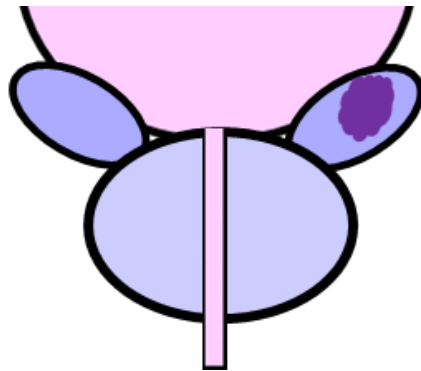


*External beam + brachytherapy boost
(PSA) Prostate Specific Antigen

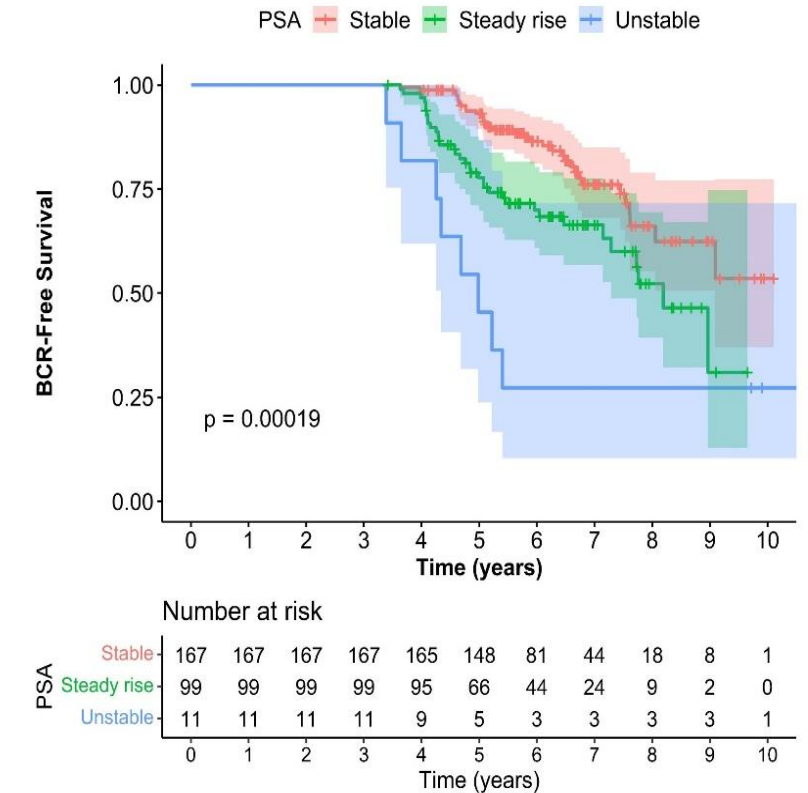
EARLY PSA DYNAMICS PREDICT LATER BCR

Validated in multiple cohorts

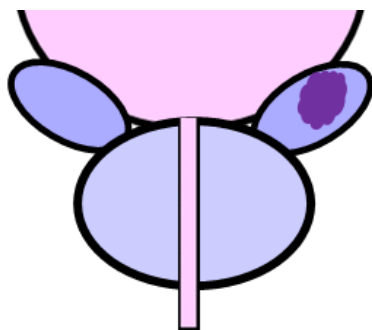
No clear association with any baseline clinical variable



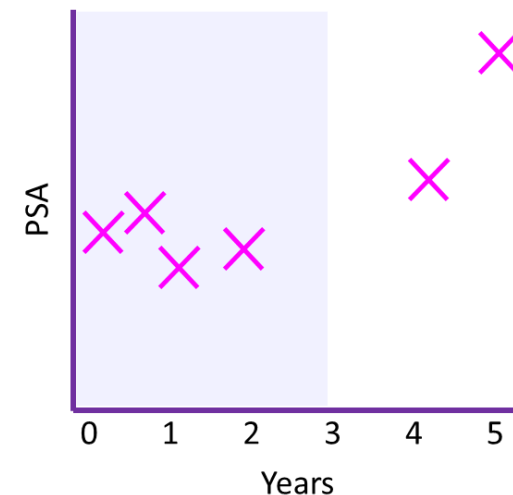
A result of incidental differences in radiotherapy dose?



Dose outside prostate → BCR



Early follow-up PSA → predict BCR



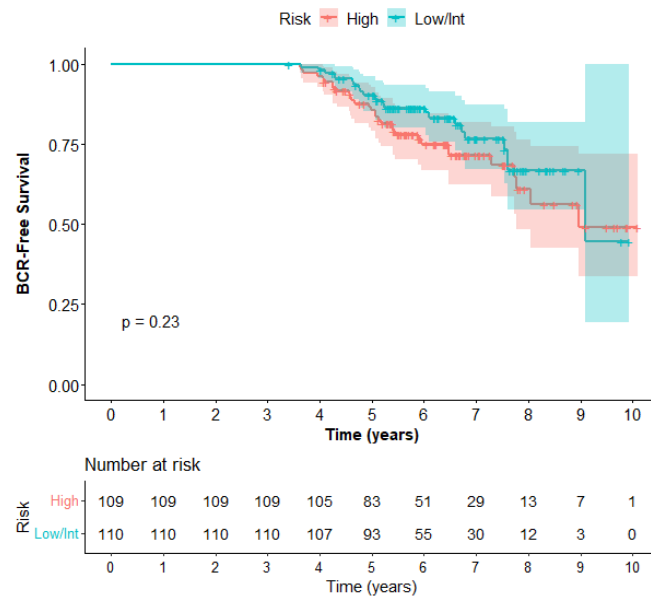
Association between dose and short-term follow-up PSA?

Incorporate sparse, irregular time-series data into Gaussian Process informed VBA

METHOD

Data (N=219)

- ✓ Planning CT + dose distribution + repeat PSA
- × BCR or lost-to-follow-up within 3-years
- ✓ BCR similar between risk-groups

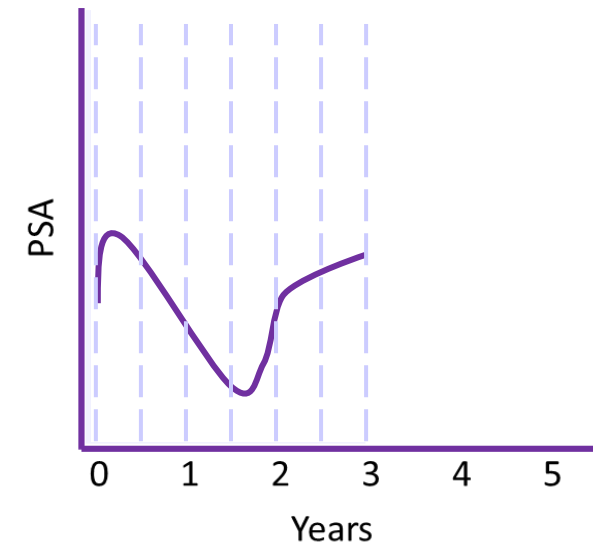


PSA

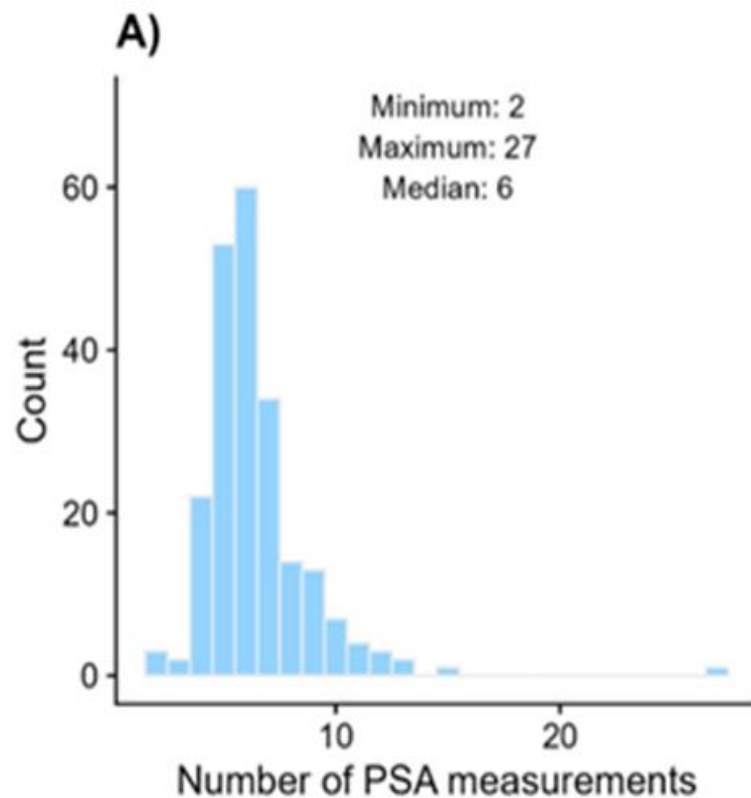
PSA data sporadic and irregular

Gaussian Process (magmaClustR)¹

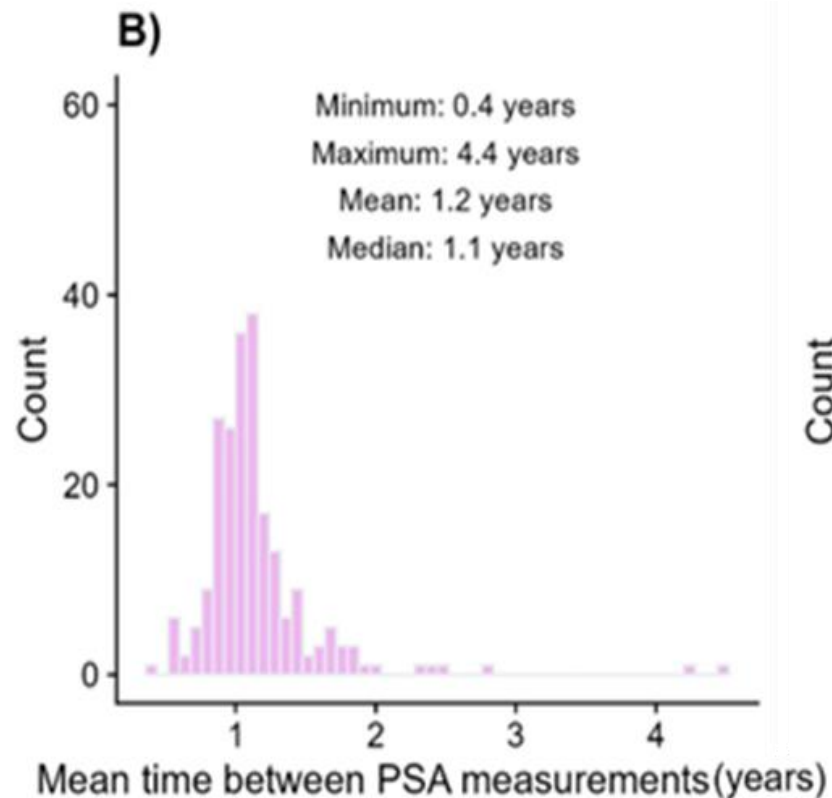
6-monthly posterior mean → interpolated PSA



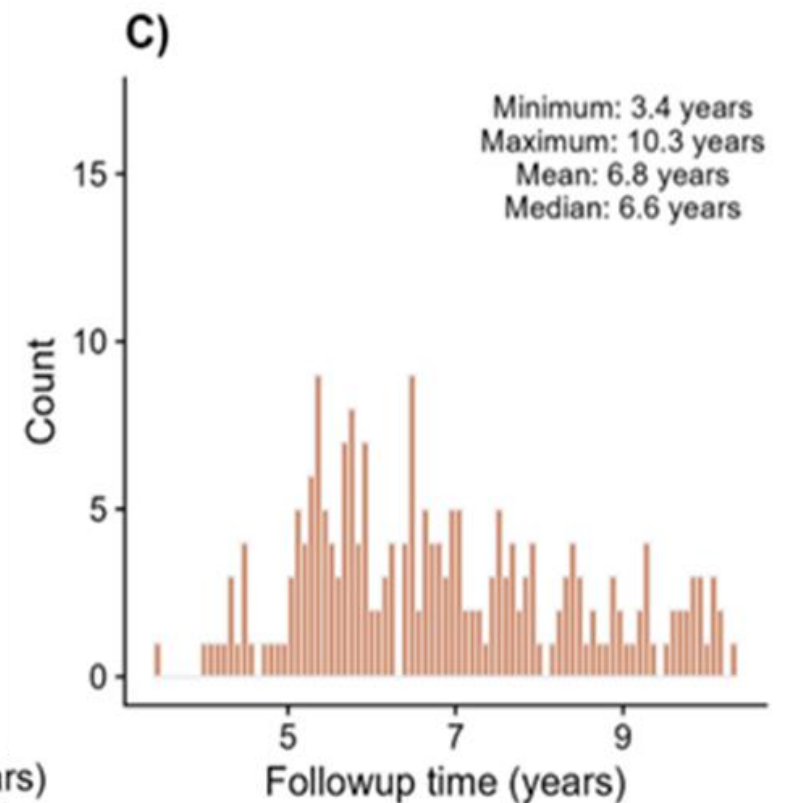
RESULTS: PSA DATA



Between 2 and 27 readings

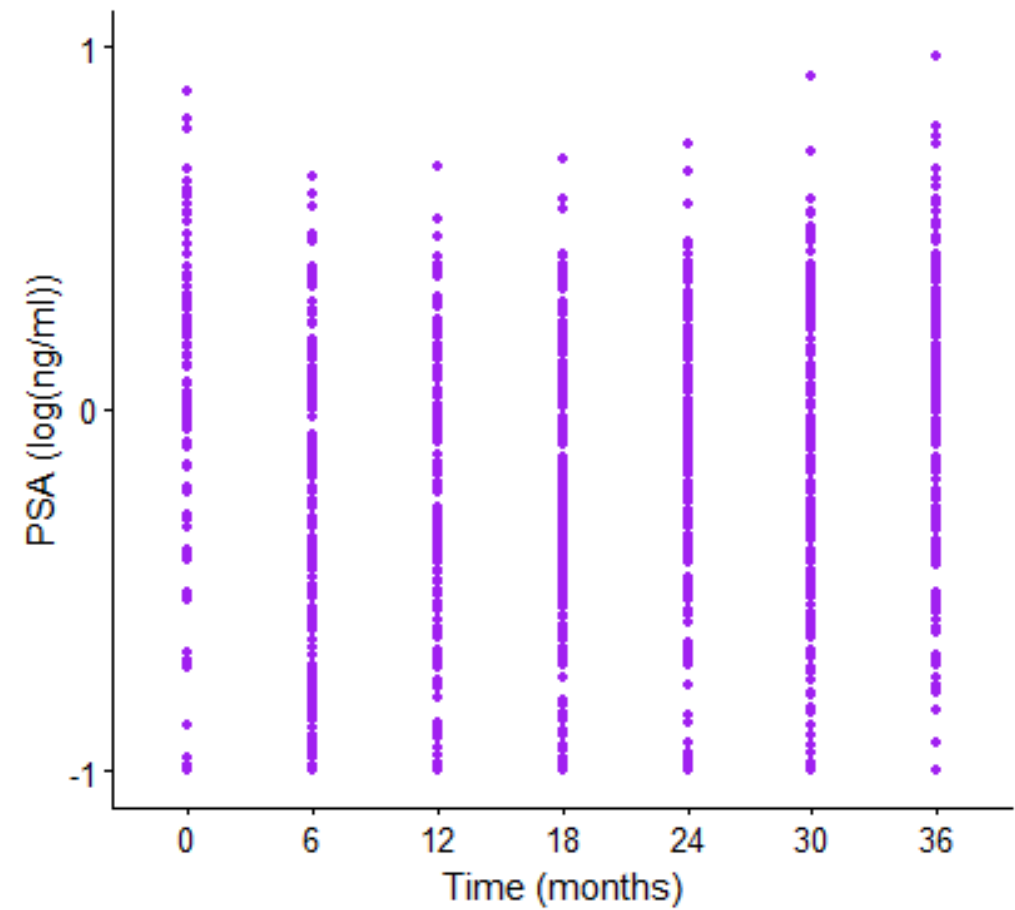
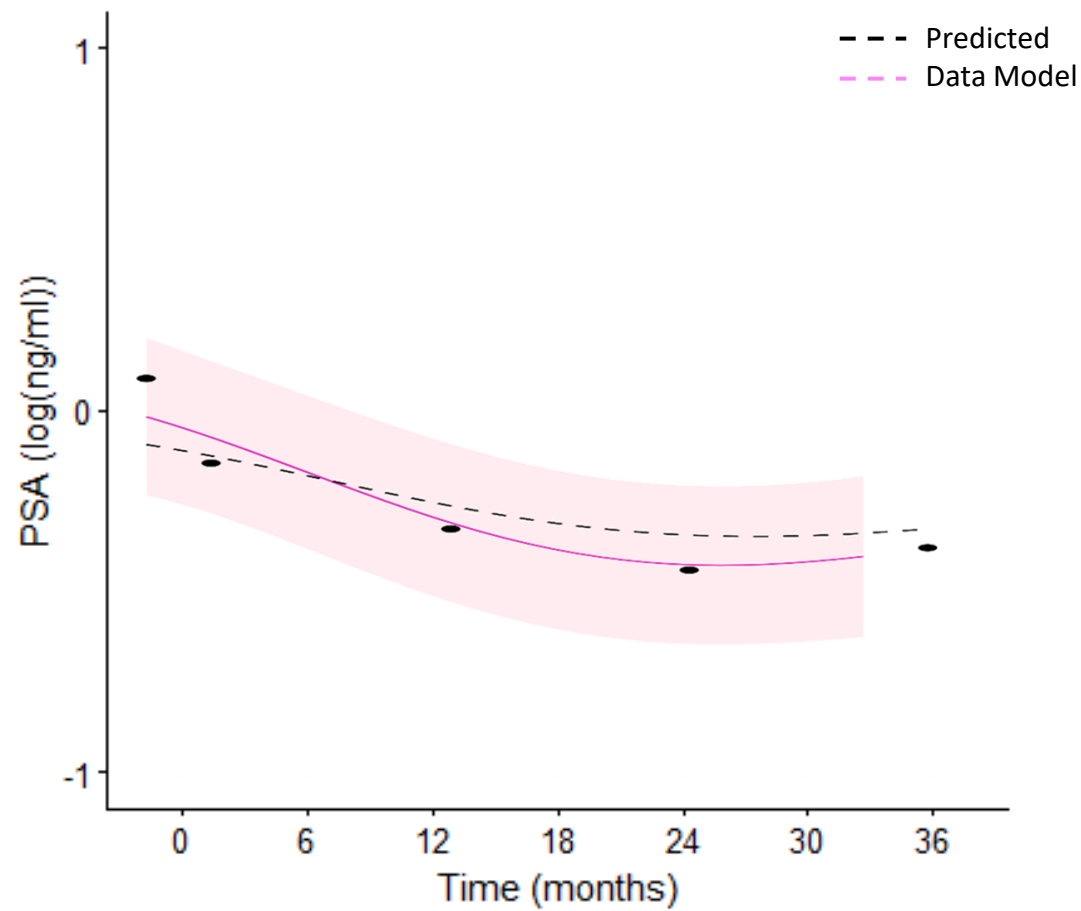


Taken every 5 months to 4.4 years



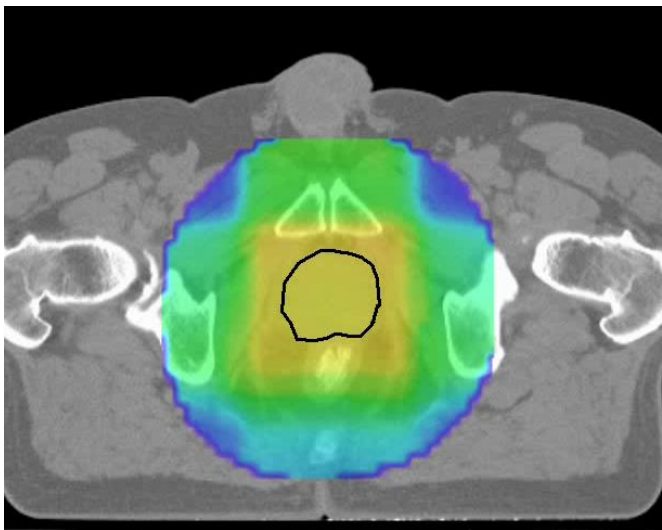
For between 3.4 and 10.3 years

RESULTS: INFERRED PSA

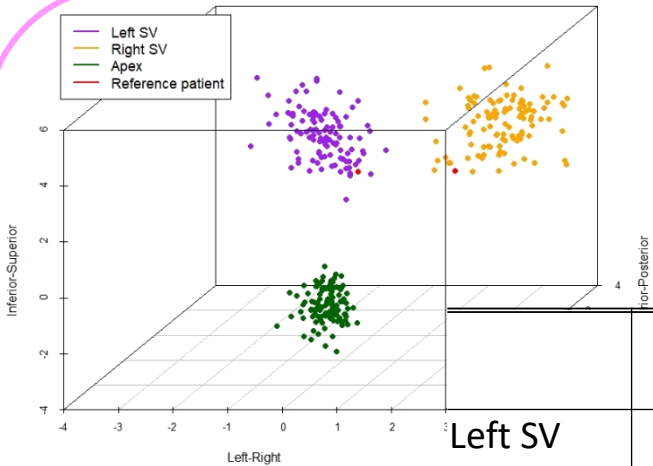


METHOD: VBA

GP informed 6-monthly PSA → Association with dose



Deformably register CTs
Align planned dose distributions (center on prostate)

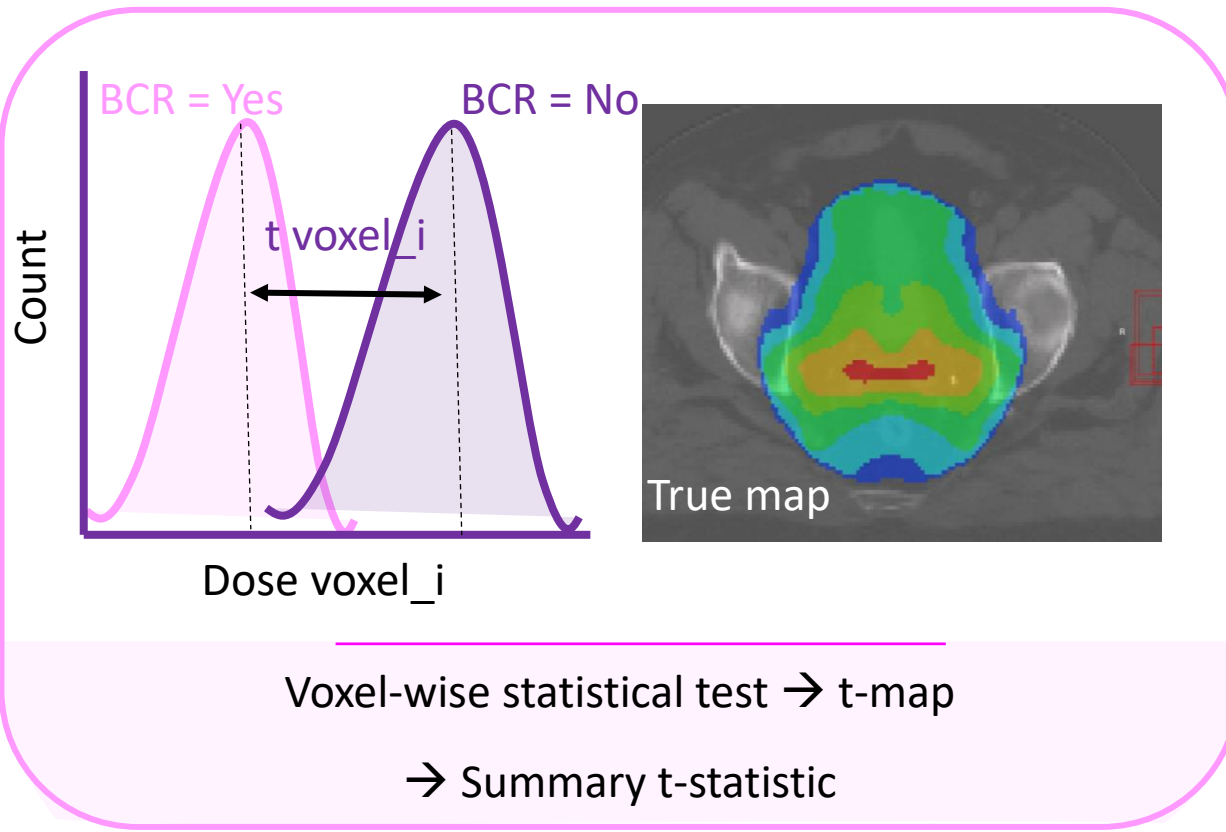


	Standard Deviation (cm)		
	LR	AP	SI
Left SV	0.48	0.58	0.90
Right SV	0.49	0.54	0.91
Apex	0.16	0.65	0.63

Target registration error → Seminal vesicles + apex
→ blur dose

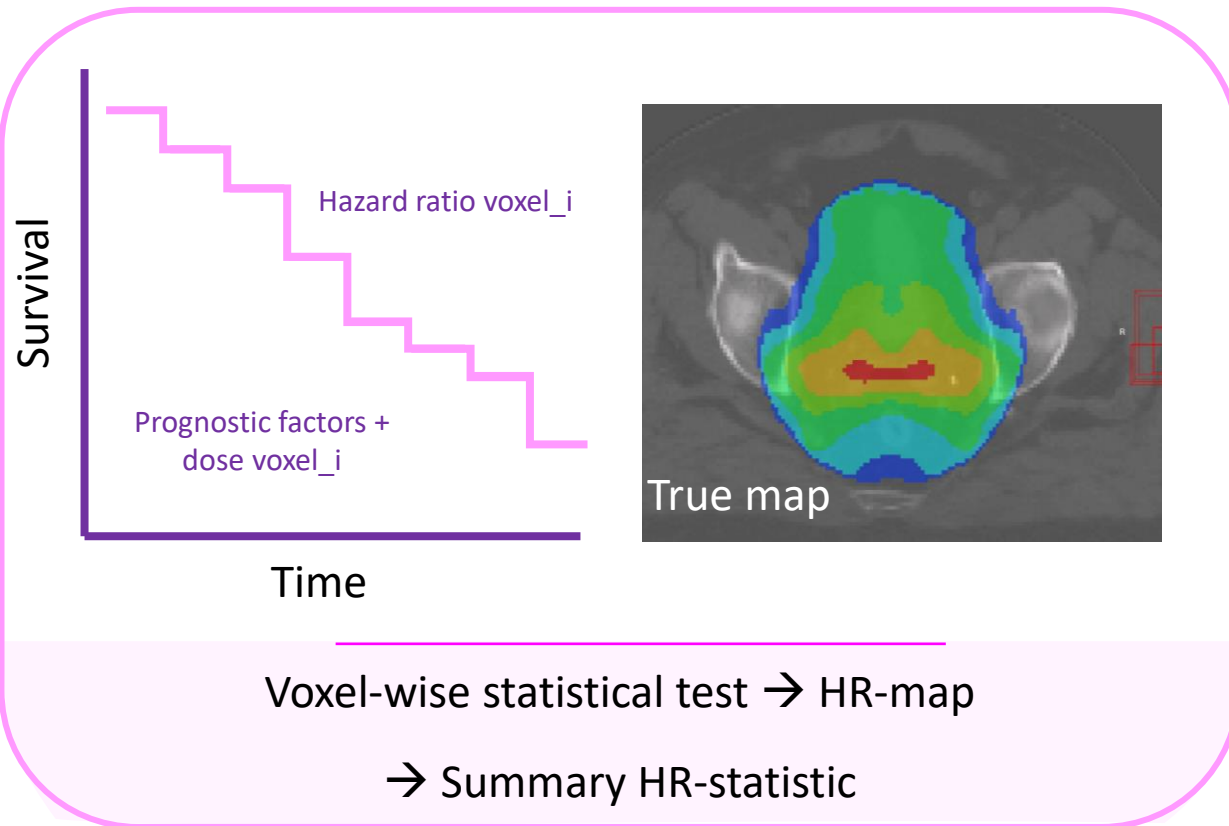
VOXEL BASED ANALYSIS

Outcome → Association with dose



VOXEL BASED ANALYSIS

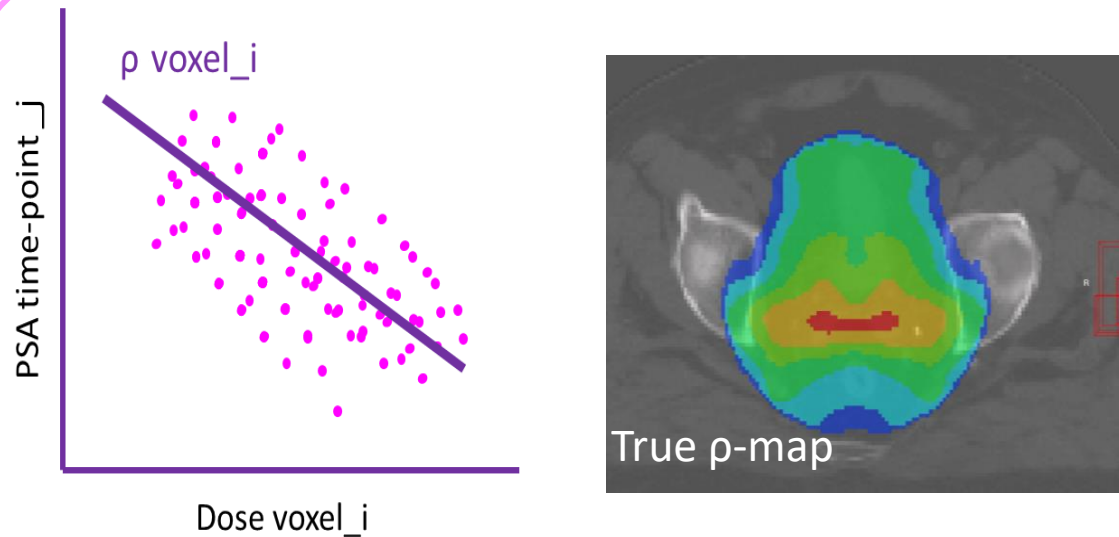
Outcome → Association with dose



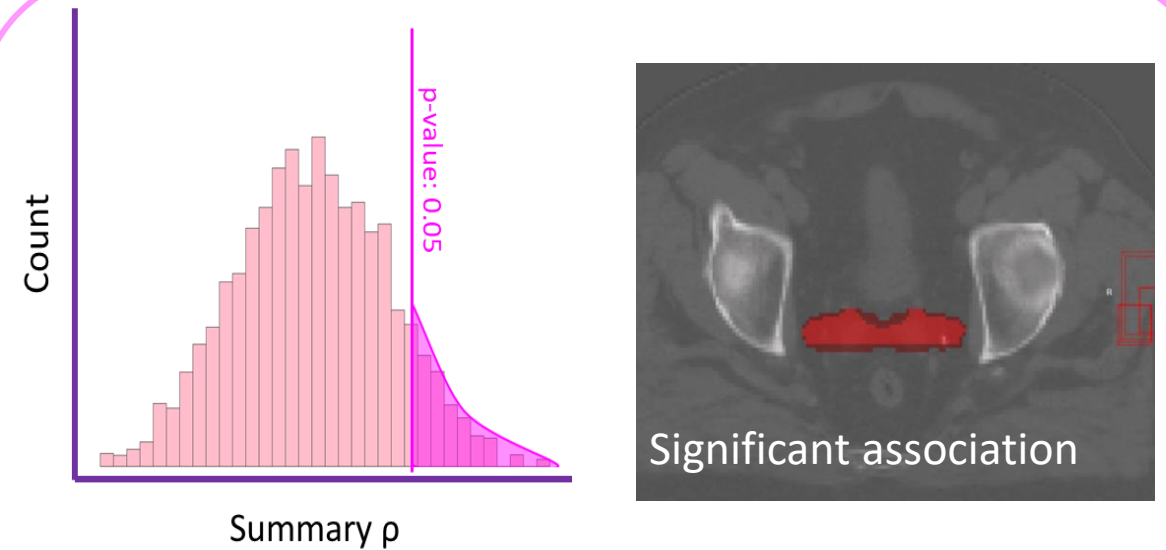
METHOD: VBA

GP informed 6-monthly PSA → Association with dose

For each PSA time-point:



Voxel-wise Spearman's rank → p-map
→ Summary p-statistic

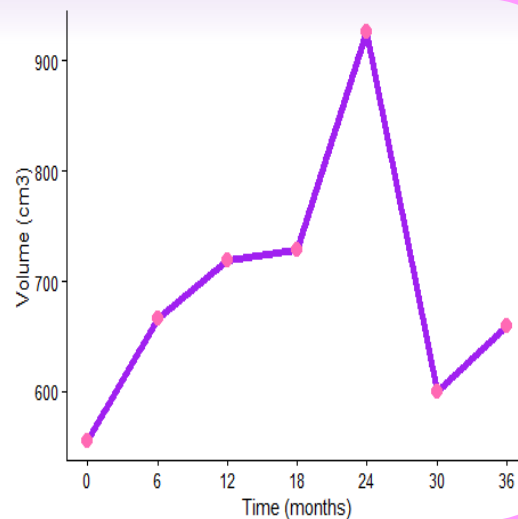


Permute + recalculate summary p → Threshold true p-map
→ Significant association

RESULTS: VBA

Significant correlation between planned dose and PSA at defined time-points

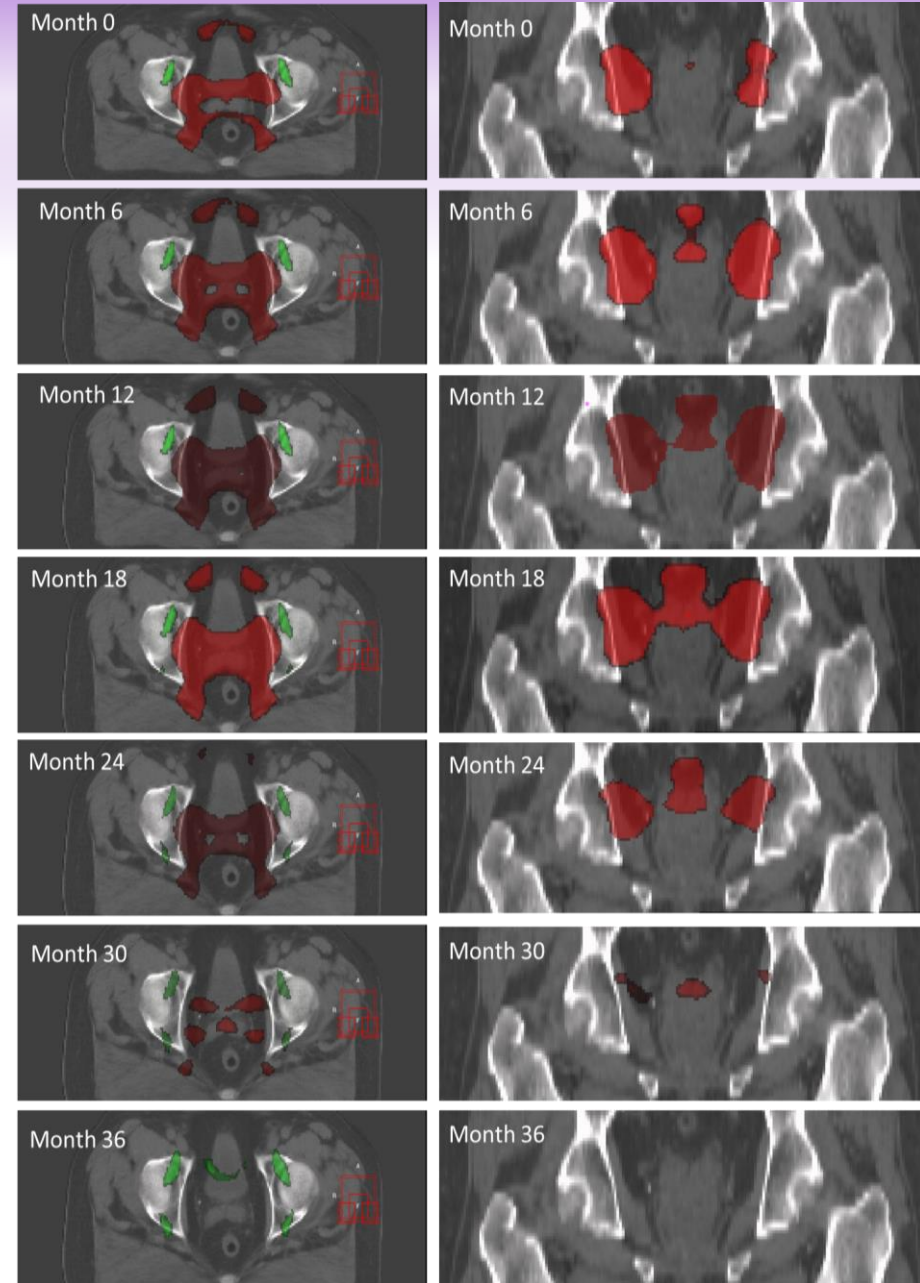
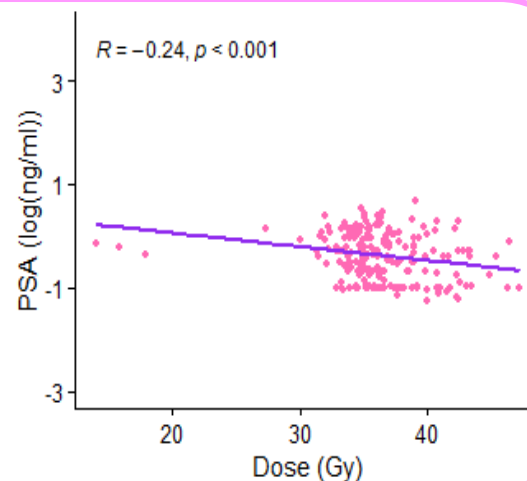
Volume grows from $\sim 300\text{cm}^3$ at 0-months to $\sim 900\text{cm}^3$ at 24-months



Higher PSA \rightarrow lower dose

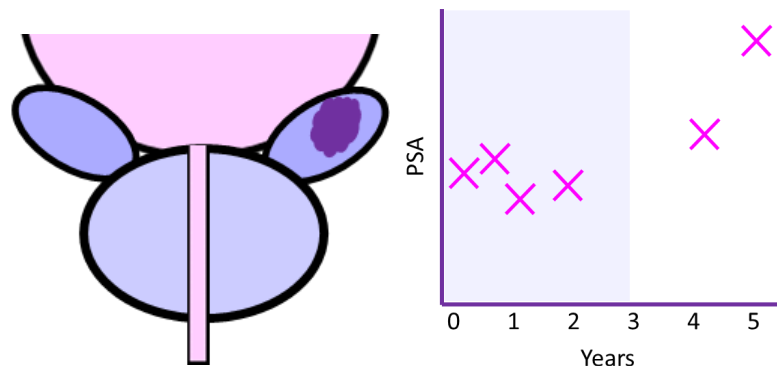
Covers seminal vesicles \rightarrow underdosage

No clear correlation with baseline clinical variable



SUMMARY

Incorporate sparse, irregular time-series data into Gaussian Process informed VBA



Association between dose and short-term follow-up PSA



Higher PSA associated with lower dose outside of prostate → underdosing?

Volume of association grows between 0 and 2 years → Importance of early follow-up PSA

- Impacted by hormone therapy?
- BCR within 3-years of radiotherapy?
- Dynamic information?



The University of Manchester




The Christie
NHS Foundation Trust

**MANCHESTER
CANCER
RESEARCH
CENTRE**

Dr Alan McWilliam
Prof. Marcel van Herk
Dr Conor McGarry
Dr David Wong
Prof. Ananya Choudhury
Prof. Peter Hoskin
Dr Kim Reeves
Dr Eliana Vasquez Osorio
Dr Andrew Green

The RRR and Christie teams



 @janeshortall1
@RT_physics

Risk		
High		109 (49.8%)
Low/Int		110 (50.2%)
Age (years)		
Mean (SD)		68.3 (6.05)
Stage		
Median [Min, Max]		2.00 [1.00, 3.00]
Gleason grade		
Median [Min, Max]		7.00 [6.00, 10.0]
ADT		
Yes		63 (28.8%)
No		156 (71.2%)
Base PSA (ng/ml)		
Mean (SD)		18.7 (18.9)
Follow-up time (years)		
Mean (SD)		6.85 (1.61)