Big-RT: Big Data Analysis to Identify Combinatorial Predictors of Radiotherapy Toxicity for Personalised Treatment in Prostate Cancer Patients

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Background

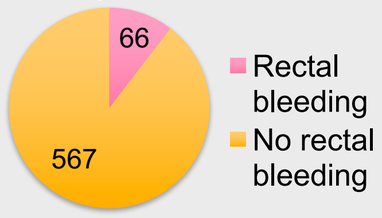
- ~ ⅔ of cancer patients will receive radiotherapy (RT).
- Up to 20% experience **long-term RT-induced toxicity**.
- **Problem:** no stratification by risk of side effects, which limits the ability to personalise treatment.
- **Challenge:** The pathogenesis of RT-induced toxicity is complex and multi-factorial, yet most **prior work focused on isolated data types** and standard statistical techniques, with limited success.

Aim

To identify multi-parametric predictors of *late* RT-induced rectal bleeding by developing novel machine learning techniques that **fully integrate** clinical, dosimetric, and genetic data from the CHHiP prostate RT-fractionation trial (CRUK/06/016)[1,2]**.**

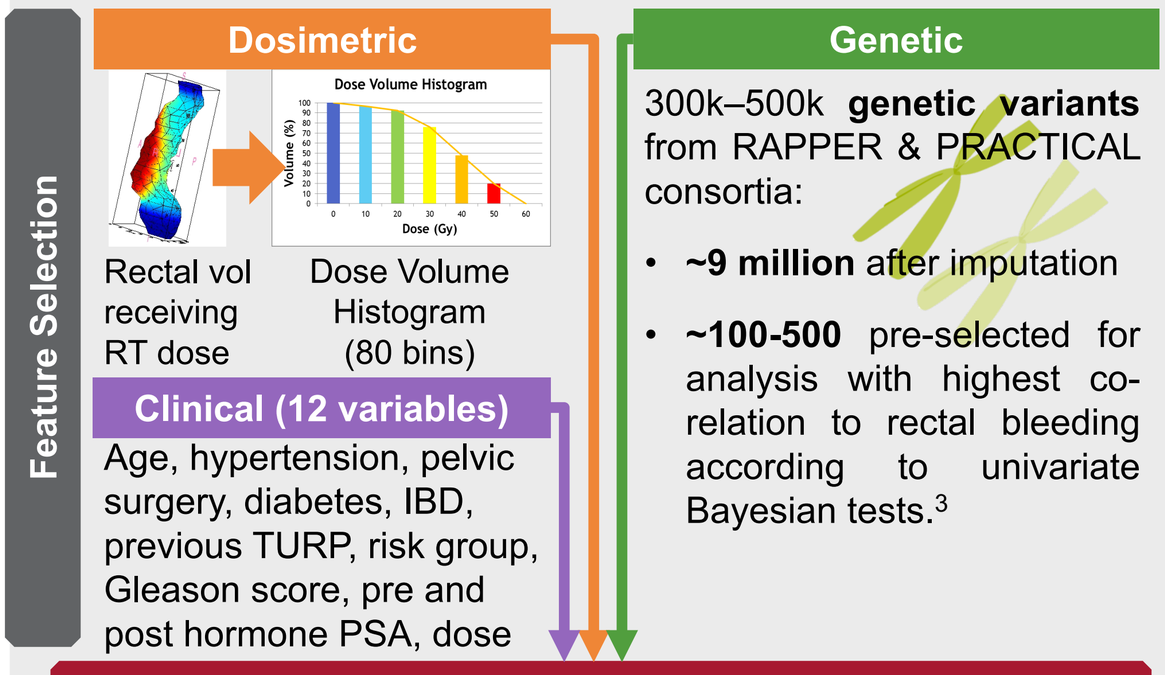
Data

- **3,212** patients recruited → **721** have all data types.
- 88 patients excluded if rectal bleeding information is missing for >3 time points and/or had heamorroids and/or rectal bleeding prior to radiotherapy.
- **633 patients eligible for analysis.**
- Rectal bleeding defined as having grade ≥ 2‡ @t ≥ 12 months.



‡: Moderate rectal bleeding (simple out-patient management)

Methods



Results

Fig 1. *Top*: Median (AUROC) performance scores for models using clinical, genetic and dosimetric factors. Black lines indicate the range of scores for our 10-fold cross validation. *Bottom*: Results using subsets of the data and **Naïve Bayes**, **our best performing model. The strongest predictions are achieved by jointly analysing all data types.**

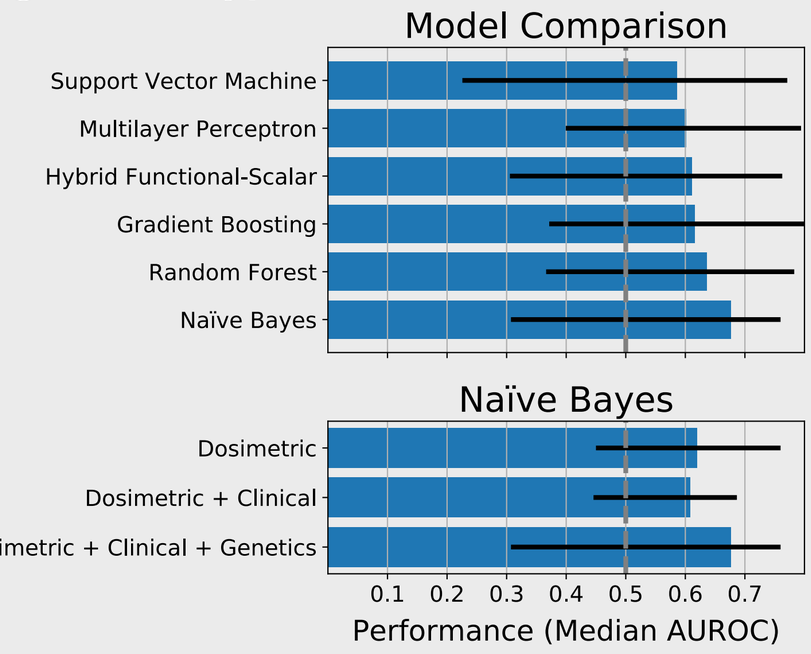
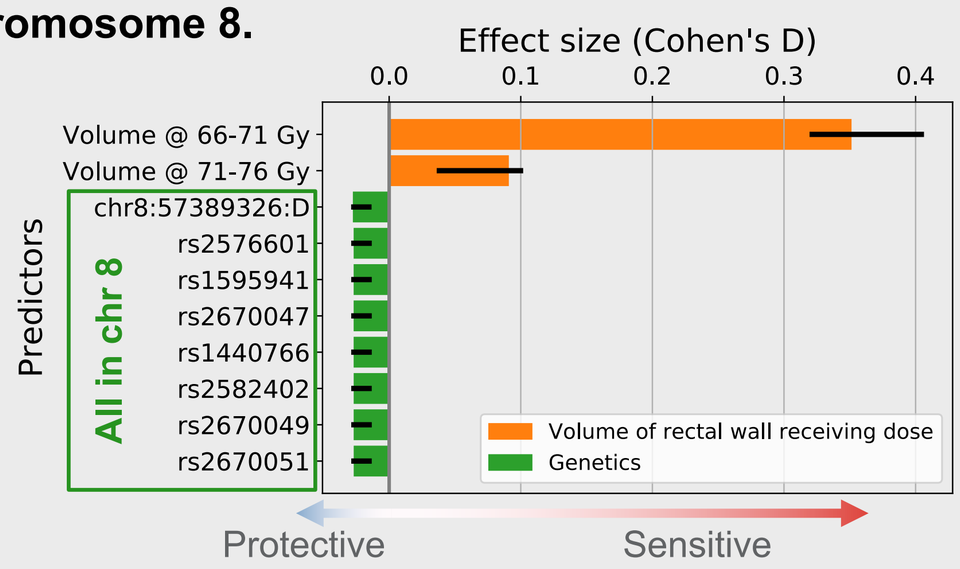


Fig 2. Strength of association to late RT-induced rectal bleeding for our top 10 predictors for the Naïve Bayes model using all data types. Genetic features shown were selected in at least 9 out of 10 folds. **Higher risk of rectal bleeding was associated with an increase in rectal volume receiving 66-76Gy, whilst lower risk was linked to genetic variants in a region of chromosome 8.**



Conclusions

- Identified novel combinatorial markers predictive of RT-induced rectal bleeding.
- Markers must be validated on independent dataset.
- Techniques developed here could be applied to other tumour types treated with radiotherapy.

References

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