A Predictive Ensemble Learning Framework for Breast Cancer Radiotoxicities at 2 Years

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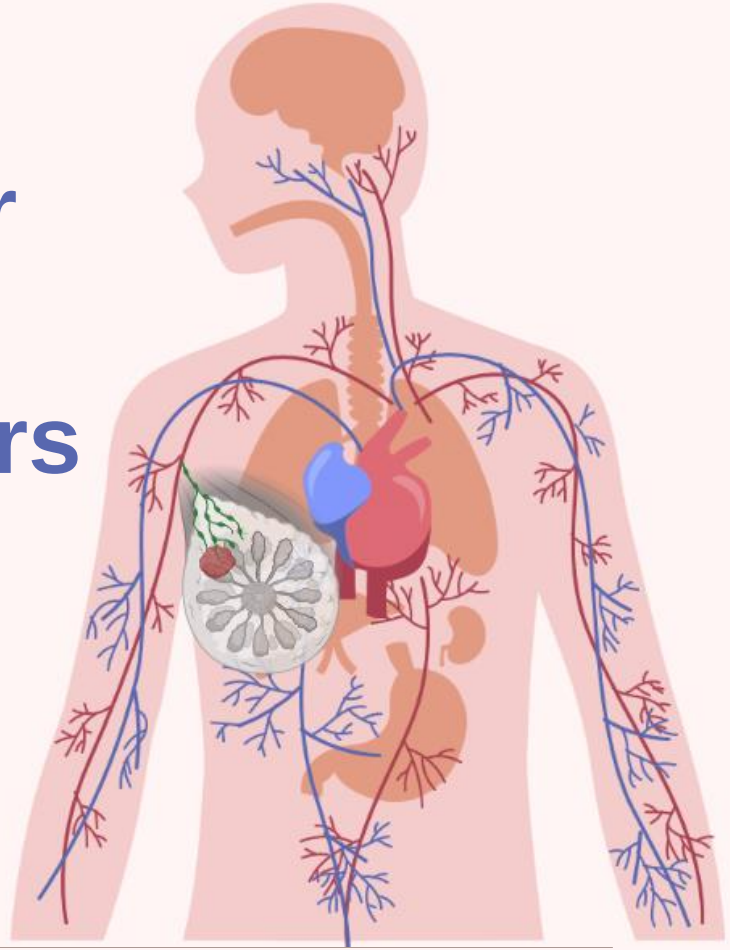

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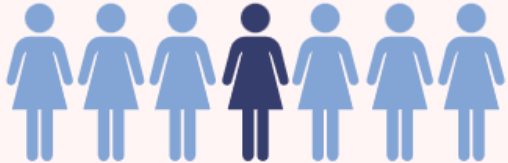
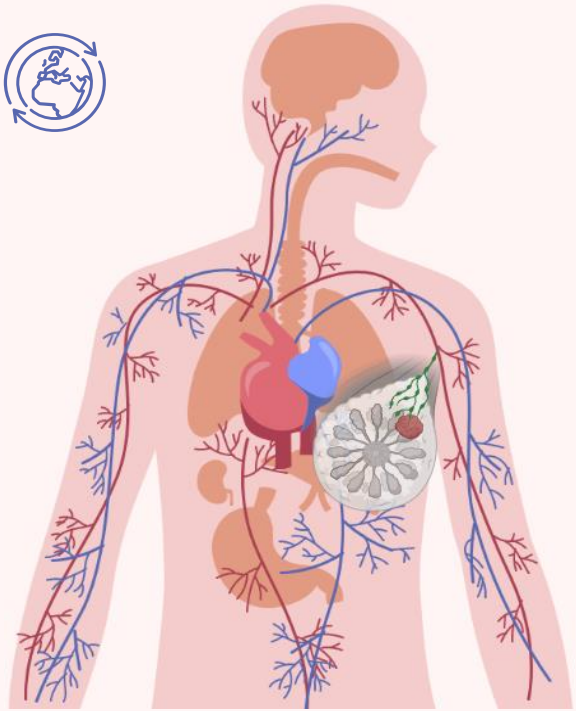
Breast Cancer

Lifetime Risk

1 in 7 UK females will be diagnosed [1]

1 every 10 mins [2]





Treatment

1. ~ 90% undergo surgery [3]
2. Systemic / chemo / hormonal / targeted
3. **> 67% get RT(radiotherapy) post-op [4]**

Radiotherapy

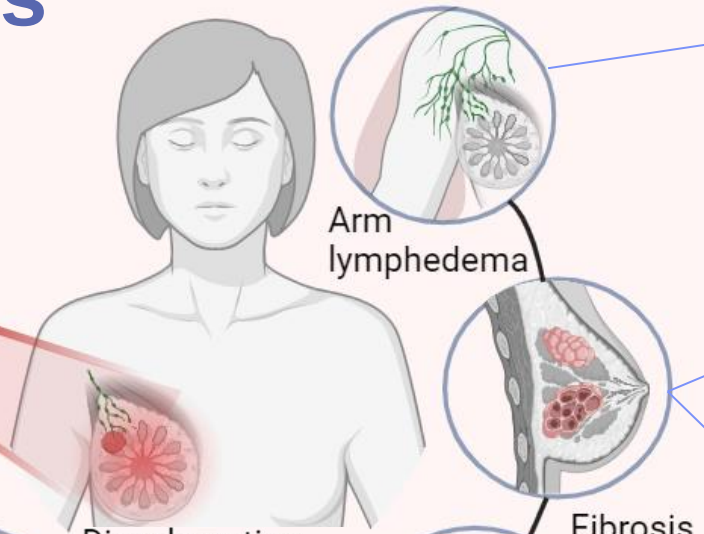
Ionising radiation => DNA damage

Decreases risk of:

- recurrence by 50% at 10yrs [5]
- Mortality by 20% at 15yrs [6]

Radiotoxicities

Radiotherapy (RT)



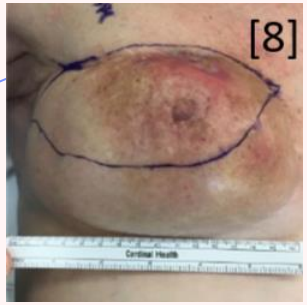
Arm lymphedema

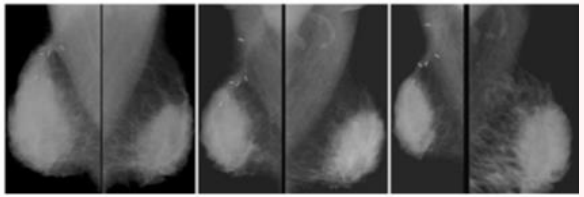
Fibrosis

Discolouration + shape variability

Telangiectasia + Pruritus

Inflammation + Pain



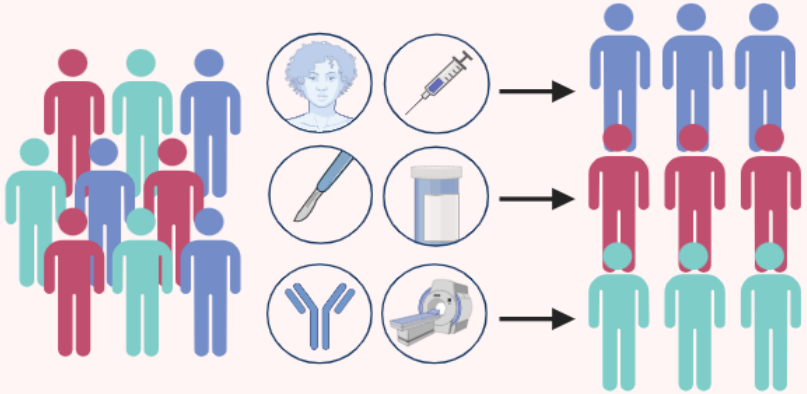


RT Induced side effects[1] ↓Quality of life post-RT

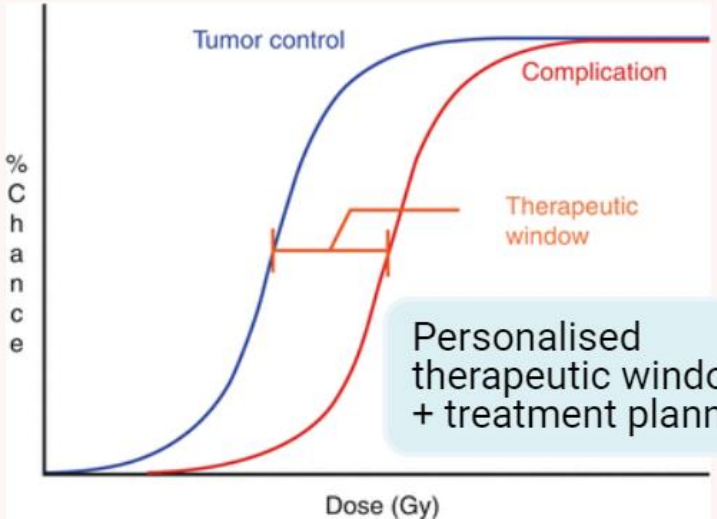
Proposed approach

Machine Learning

- leveraging statistical power to analyse complex datasets
- Pattern identification
- Supervised learning
- Unsupervised learning



Risk stratification[11] + adapting therapy combinations



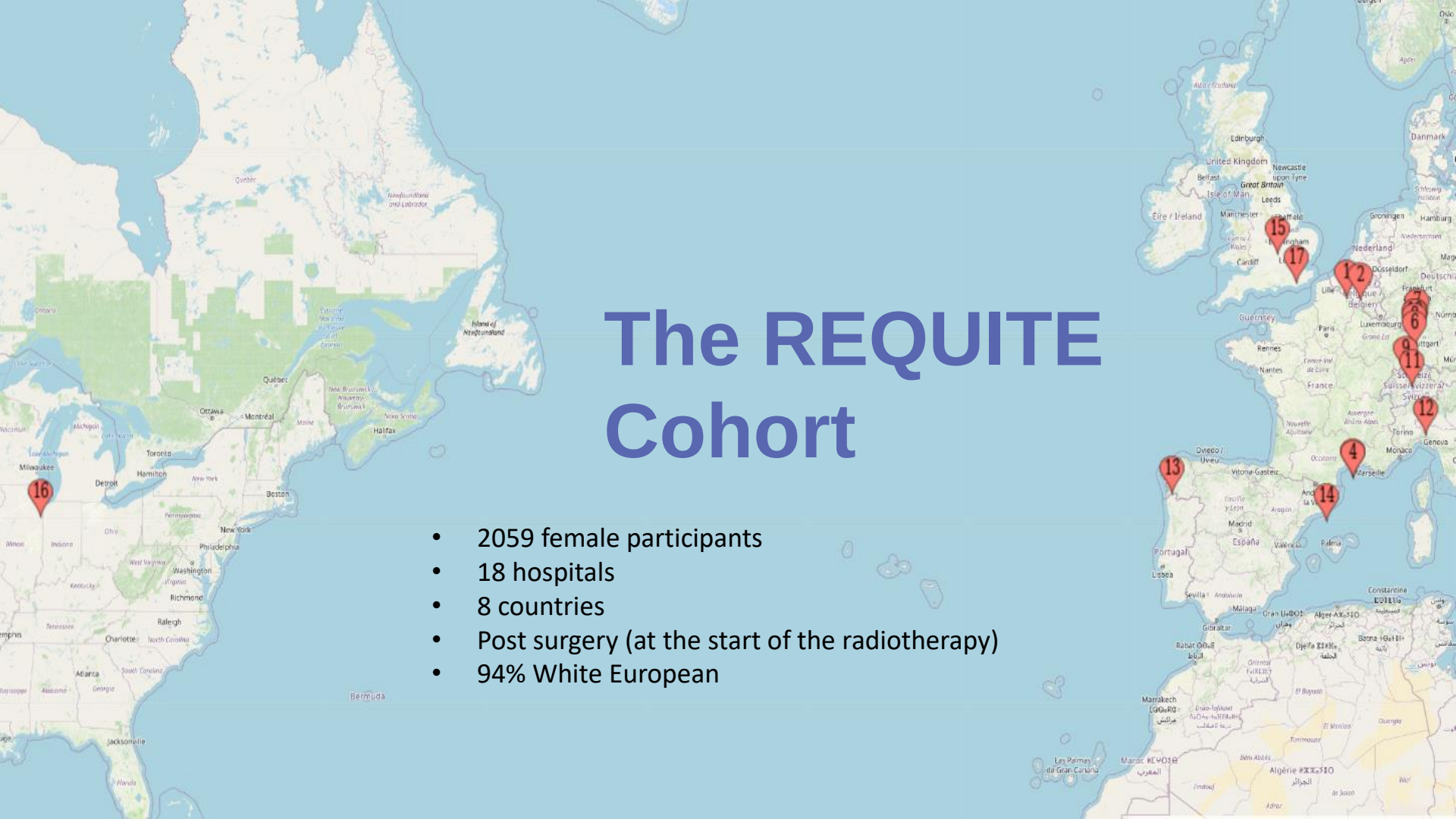
Personalised therapeutic window[10] + treatment planning

Improved outcomes + prognosis

Reduced radiotoxicity → ↑Quality of life post-RT

Aim:

to develop and evaluate an **ensemble ML framework** that integrates multiple algorithmic predictions to **predict long term (at 24 months) breast cancer radiotoxicities**



The REQUITE Cohort

- 2059 female participants
- 18 hospitals
- 8 countries
- Post surgery (at the start of the radiotherapy)
- 94% White European

REQUITE Cohort:
2060 Patients
83 predictors
9 radiotoxicty endpoints

Preprocess:
1. Splitting into training and testing
2. KNNimputing
3. One Hot Encoding
4. Normalising

Feature selection:
- Visualisation
- Recursive feature elimination

Multivariate Adaptive Regresssion Splines

AdaBoost

Random Forest

Support Vector Machines

- Cross Validation
- Confusion Matrix
- Hyper-Parameter tuning

Evaluate and compare 4 algorithm performances

Stack performances to **Ensemble** predictions to form single model and score

Methods Overview

1) Preparation & variable selection

REQUITE Cohort:
2060 Patients
83 predictors
9 radiotoxicty endpoints

Exclusion criteria:
- Pt records lacking outcome endpoint
- Variables with more than 10% missing data

Category	Number of Variables
Patient characteristics	8
Medical history	17
Surgery-specific	8
Tumour	11
systemic treatment details	5
Radiotherapy trt	20
Baseline radiotoxicity	13

Preprocess:
1. Splitting into training and testing
2. KNNimputing
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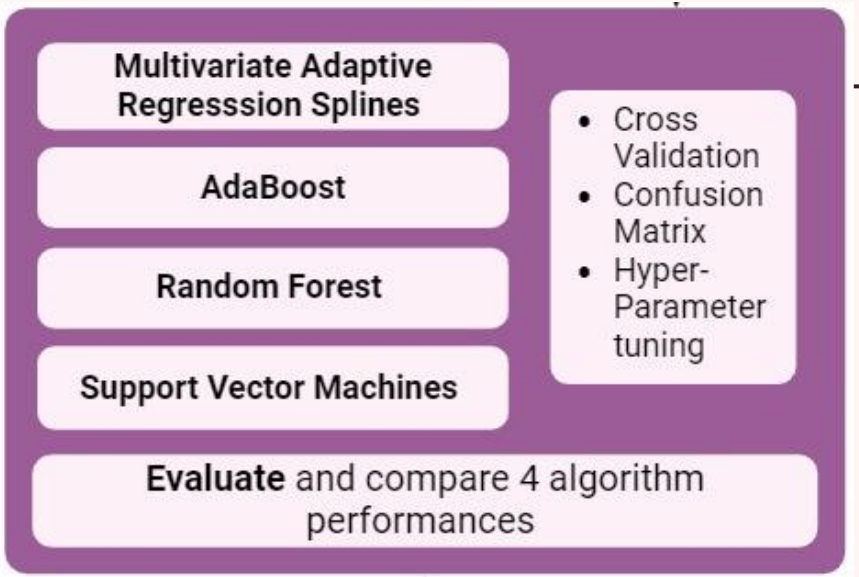
4. Normalising

Feature selection:
- Visualisation
- Recursive feature elimination

2) Modelling

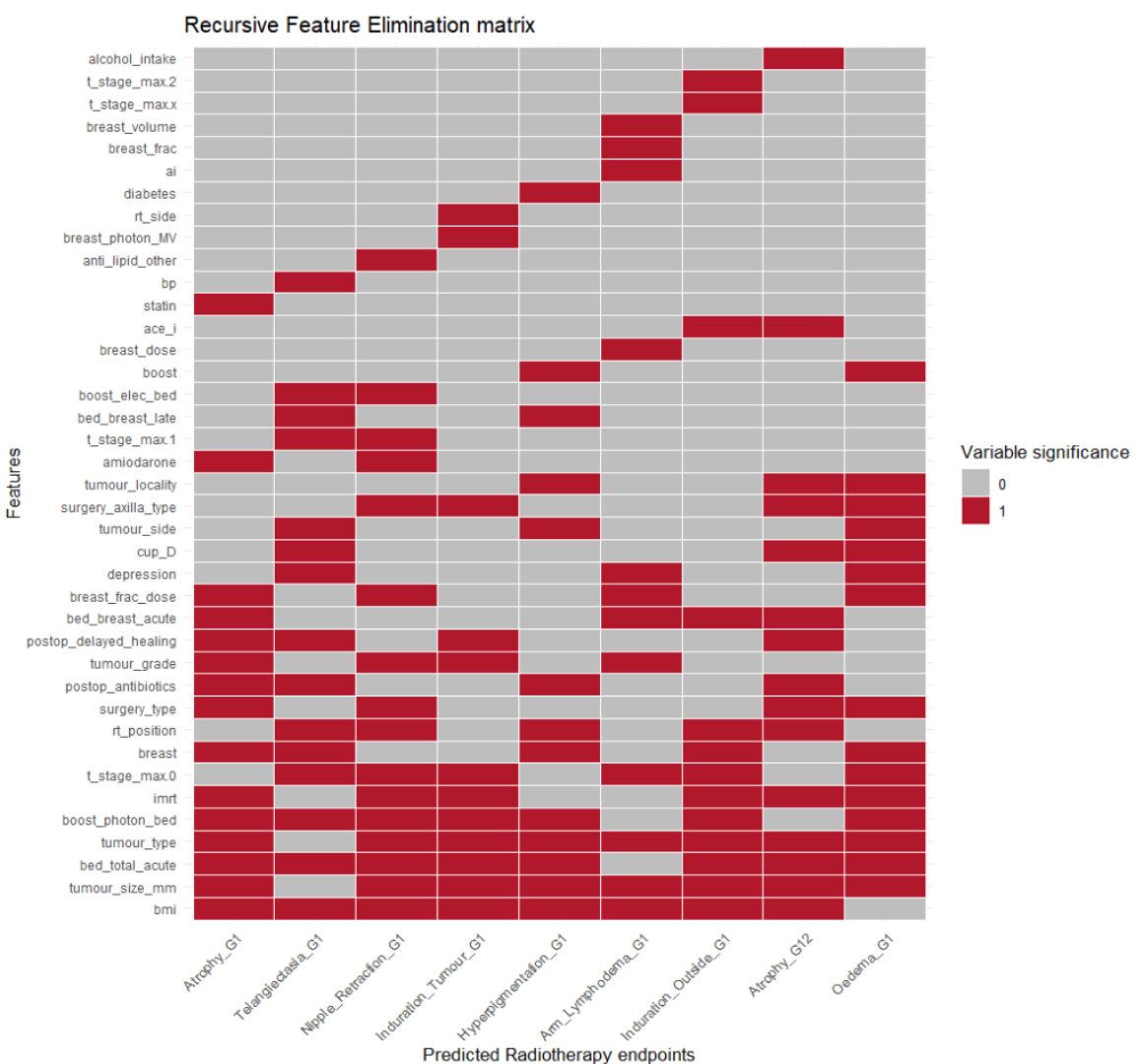


Stack performances to **Ensemble** predictions to form single model and score

Comparing 4 ML models

- **AUROC**
- **Sensitivity**
- **Specificity**

RESULTS



Recursive feature elimination

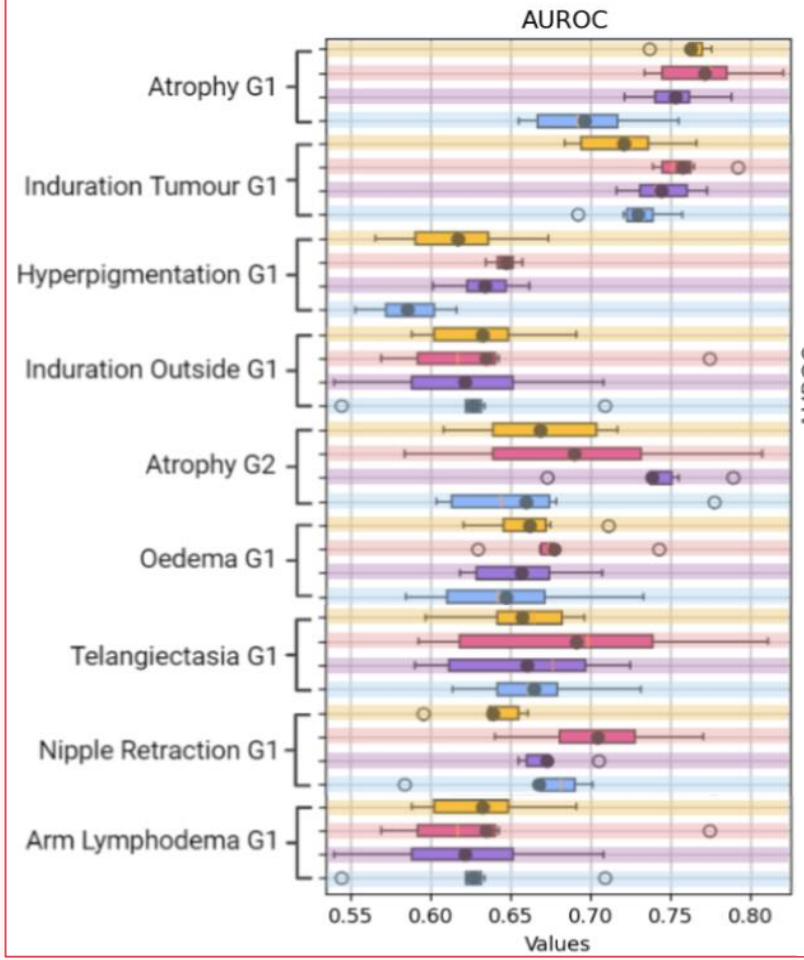
Each endpoint = top 15 features with the highest predictive power (out of 85)

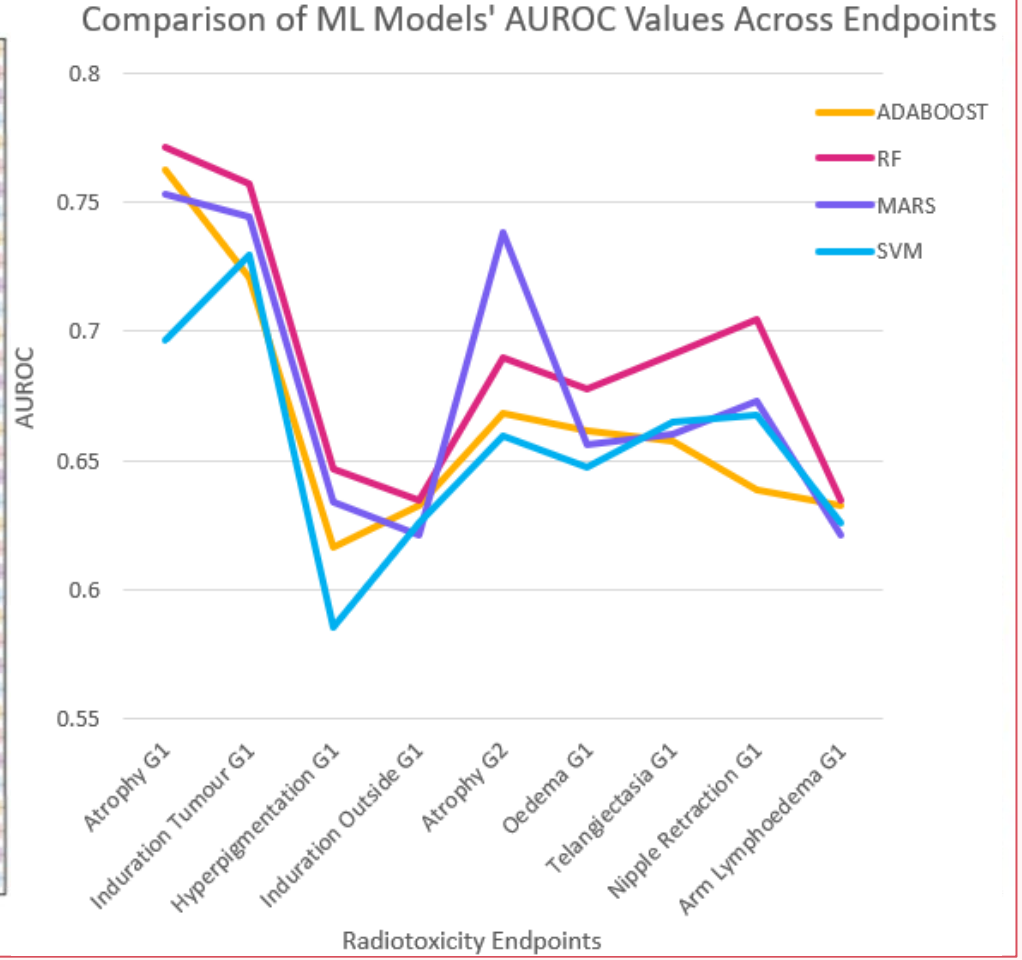
39/85 <- were in top 15 for all 9 endpoints

3 were significant predictors for 8 out of 9 endpoints

13 features uniquely significant

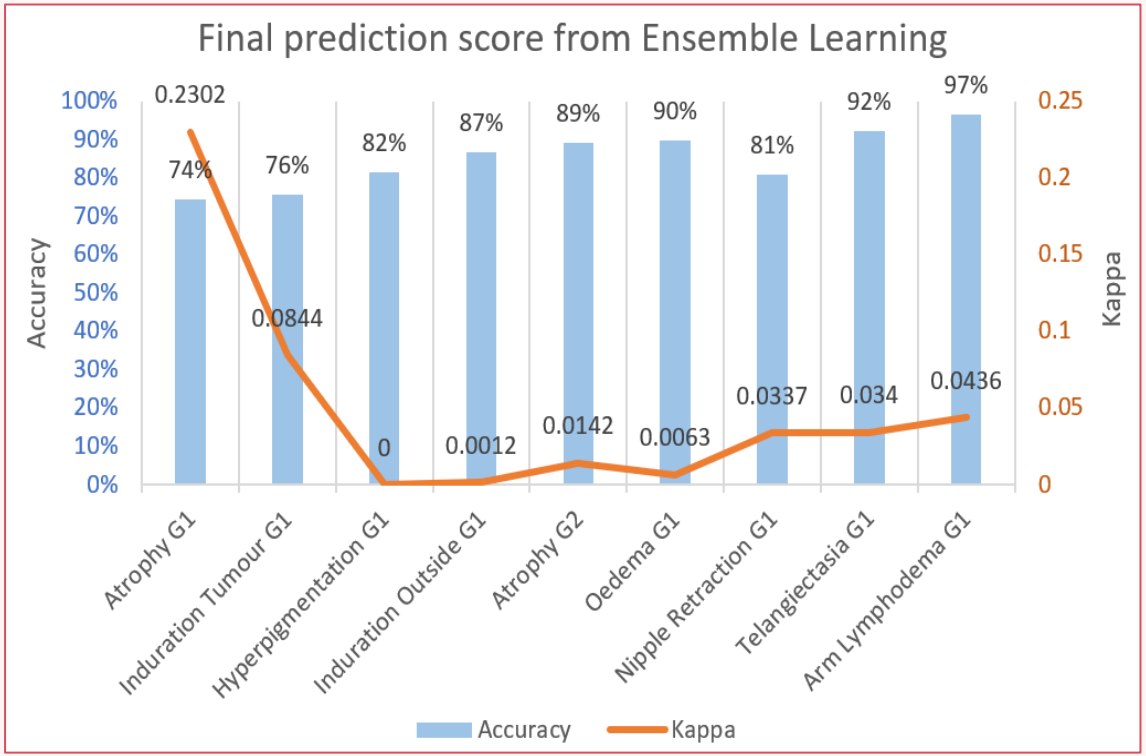
Comparative Analysis of Machine Learning Model Performance Across Radiotoxicity Endpoints





Comparative Performance of Machine Learning Models across 9 radiotoxicity endpoints

Ensemble predictions



AUROC (0 to 1)

- Summarises the trade-off between sensitivity and specificity

Accuracy (0 to 1)

- overall correct predictions,

Kappa (-1 to 1)

- Measure of agreement beyond chance

Discussion

Current landscape

Increase interpretability and explainability

- SHAP (SHapley Additive exPlanations)
- LIME (Local Interpretable Model-agnostic Explanations)

Limitations and next steps:

- Class imbalance => could use SMOTE
- Inclusion of SNPs
- Overfitting => Lasso or ridge regularisation
- 94% White European dataset =>
- External Validation

A prediction model is “a snapshot in place and time, not fundamental truth" (Lezzoni, 1999)

Thank you!

Any questions?

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