Prognostic modelling of time-to-event endpoints in Prostate Cancer

Prostate cancer is among the most common cancers for men globally, accounting for 13% of cancer diagnoses in the male population each year and effecting one in eight men in Ireland. Radical prostatectomy (RP) is the primary treatment option but fails in 20-40% of patients, who subsequently develop biochemical recurrence (BCR). The focus of this study is in the prediction of BCR and investigating opportunities for inclusion of genetic attributes alongside routine clinical information for improved predictive performance, and towards a clinically useful precision medicine decision tool.

Analyses were carried out on a publicly available data source with a clinical cohort of 198 patients with BCR-free time information, 140 of which also had genetic mRNA data. Predictive models used in the benchmarks included tree-based methods such as random survival forests (RSF) and boosted and regularized Cox proportional hazards modelling. The impact of various aspects of the machine learning pipelines and the relative contribution of candidate feature for prediction of BCR-free survival were assessed from both pre-RP and post-RP perspectives. Comparative analyses with state-of-the-art predictive tools and traditional modelling approaches were also carried out.

Preliminary cross-validated results indicated that inclusion of mRNA information yielded increased prognostic performance with a 5% increase in C-index (Cross-validated C-index: 0.76 vs. 0.71; 95% Confidence Interval: (0.010, 0.011)). Post-operative prediction outperformed pre-operative performance (0.80 vs 0.73; (-0.14, -0.01)). Excluding mRNA variables, no statistically significant difference was found between Cox models and RSF. When including mRNA variables, the Cox models outperformed RSF (CV C-index: 0.74 vs. 0.63; 95% CI: (0.04, 0.19)). These findings provide a good basis for discussion on the potential integration of precision medicine tools for management of prostate cancer.