PREDICT: Prostate – a Novel Individualised Prognostic Model for Non-metastatic Prostate Cancer with the Potential to Reduce Overtreatment of Lower-risk Disease

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Purpose: To develop an individualised prognostic model for non-metastatic prostate cancer (PCa) that contextualises PCa-specific mortality (PCSM) against other cause mortality, and estimates the survival benefit of treatment and to assess the potential impact of the model on clinician decision-making.
Methods: Using records from the UK National Cancer Registration and Analysis Service, data were collated for 10 089 men diagnosed with PCa between 2000 and 2010 in eastern England. Median follow-up was 9.8 years with 3829 deaths (1202 PCa-specific). Data were randomly split 70:30 into model development and validation cohorts. Separate multivariable models were built for 15-year PCSM and non-prostate cancer mortality (NPCM) using fractional polynomials. Discrimination and calibration were assessed by Harrell's C-index and chi-squared goodness-of-fit, respectively, within the UK validation cohort and an independent Singaporean dataset of 2546 men. An online clinician survey using hypothetical vignettes was developed using Qualtrics® software and distributed to professionals in urology and oncology.
Results: A multivariable model called 'PREDICT: Prostate' was constructed combining age, PSA, histological grade, biopsy core involvement, stage and primary treatment type, which were each independent prognostic factors for PCSM; and age and comorbidity, which were prognostic for NPCM. The model demonstrated good discrimination with C-index 0.83 (95%CI: 0.80–0.85) and 0.86 (95%CI: 0.83–0.89) for 15-year PCSM and 0.75 (95%CI: 0.74–0.77) and 0.77 (95%CI: 0.74–0.79) for overall mortality in the UK and Singapore validation cohorts, respectively. This outperformed currently endorsed international risk-stratification criteria ($P < 0.001$). Among 142 survey respondents (63.4% urologists), there was a trend towards lower rates of recommendation for treatment in men with favourable prognosis when PREDICT: Prostate estimates were shown.
Conclusion: PREDICT: Prostate is the first truly individualised multivariable PCa prognostic model built from baseline diagnostic information and the first to model potential treatment benefit on survival. The eventual web-tool should aid in patient counselling and treatment decision-making.

Exploring the Value of a Pre-trial Outlining Exercise in the POPS Trial, which Evaluated the Localising Device ProSpare in Prostate Bed Radiotherapy

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Purpose: ProSpare is a self-insertable, single use rectal obturator designed as a daily image-guidance tool for prostate and prostate bed radiotherapy. It helps to stabilise the rectum, prostate bed and seminal vesicles [1]. We evaluated the impact of the POPS pre-trial quality assurance outlining exercise and the use of ProSpare on the reproducibility of prostate bed outlining.
Methods: POPS is a randomised phase II trial comparing prostate bed radiotherapy with/without ProSpare. The study design requires that all participating consultants complete a pre-trial outlining exercise both with and without ProSpare [2]. If contouring did not adequately follow RTOG guidelines [3] the outlining exercise was repeated after personalised feedback. The gold standard outline was developed by a specialist uro-radiologist with the chief investigator. 12 investigators from 11 centres contributed to the exercise. We measured the variability between each contour set and the gold standard using the Dice Similarity Coefficient (DSC). A DSC $\geq$ 0.7 indicates good agreement [4]. DSC was calculated for each set of contours in both ProSpare and non-ProSpare groups.
Results: In the initial outlining exercise, the median DSC was 0.84 (range 0.61–0.90). 4 investigators repeated outlining with ProSpare and 7 without ProSpare. For these 11 contours the median DSC improved from 0.78 to 0.90. For the initial outlines the median DSC was similar in the Prospare groups (0.85) and the non-ProSpare groups (0.82). 8 of the 11 cases re-contoured had a DSC of more than 0.7.
Conclusion: This study highlights clinician variability in contouring for prostate bed radiotherapy. Centralised audit and review has been shown to improve reproducibility. Outlining had a similar consistency in ProSpare and non-ProSpare groups.
References
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Palliative Radiotherapy to Bladder Cancer – Futile or Utile?

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Purpose: To investigate the efficacy of palliative pelvic radiotherapy (RT) for patients with advanced bladder cancer and identify factors associated with futile treatment.
Methods: Retrospective data were collected for bladder cancer patients receiving palliative pelvic RT between 2013 and 2017. Patients were stratified and overall survival (OS) was analysed. Patients were followed up at approximately 6 weeks after RT. Death before, during or within 6 weeks of treatment was considered as a marker of receiving futile treatment.
Results: 134 patients were planned to receive palliative pelvic RT. Median age was 78 years (53–95 years). Majority had transitional cell carcinoma (89.6%) and advanced stage (stage III, IV and recurrent disease; 90%). The main indications were local control (39%), haemostasis (33%) and pain control (22%). Most common radiotherapy regimens were 20 Gy/5 fractions (38%), 21 Gy/3 fractions (36%) and 30 Gy/10 fractions (27%). About 45% of patients were of poor performance status (ECOG 3 or 4) and had significant co-morbidities (ACE-27 score 2 or 3). The median OS after last fraction of RT was 95 days (2–1042 days). 30% ($n = 40$) of patients died within 6 weeks after receiving palliative RT. More than half ($n = 73$) reported their outcomes during clinic or telephone follow-up with median follow-up time of 48 days (14–113 days). 31% ($n = 42$) of patients reported no improvement of symptoms. Patients of better performance status (ECOG 0–2) survived significantly longer than those with worse performance status [151 days (108–193 days) versus 45 days (19–70 days), $P = 0.000071$]. Otherwise, there were no significance differences between median OS with high co-morbidity, advanced stage, age or radiotherapy regimen.
Conclusion: A third of patients either did not complete RT or died within 6 weeks of treatment. Patients might not have achieved maximal benefit or suffered side-effects during this time, making this a futile treatment. Patient selection and comprehensive assessment are crucial in preventing ineffective treatment.

Multidisciplinary Inter-observer Variation using Magnetic Resonance Imaging (MRI) for Muscle Invasive Bladder Cancer (MIBC) Radiotherapy Target Definition

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