was maintained as long as the effect metric used for Cox regression had a linear correlation with the true effect metric of at least 0.50. The conclusions held if the trial cohort consisted of an expected high benefit population (22% reduced sample size), but the effect was even stronger even if the cohort was a population with modest expected benefit (31% reduced sample size).

### Standard population

- **JDL offense**
  - 2 Gy, 60 Gy, normal risk factor prevalence
  - Standard (log-rank) 744 patients
  - Model-based (Cox regression to JDL offense) 649 patients
  - Model-based (misclassified effect metric, correlation 0.80) 614 patients
  - Model-based (misclassified effect metric, correlation 0.50) 743 patients

### High benefit population

- **JDL offense**
  - 2 Gy, 67 Gy, high risk factor prevalence
  - Standard (log-rank) 218 patients
  - Model-based (Cox regression to JDL offense) 169 patients

### Low benefit population

- **JDL offense**
  - 2 Gy, 63 Gy, low risk factor prevalence
  - Standard (log-rank) 2300 patients
  - Model-based (Cox regression to JDL offense) 1587 patients

| Table 1: Standard trial design (log-rank statistics) compared to model based Cox regression. Risk factors included were: pre-existing pulmonary co-morbidity (HR = 3.27), mid or inferior tumour location (HR = 1.87), current smoker (HR = 1.02), and old age (HR = 1.58). The consequences of a misclassified effect metric were examined for correlations ranging from 0.20 to 0.46; example results are shown. |

### Conclusion

We have demonstrated that the required patient sample size for randomized trials in radiation oncology may be considerably reduced by taking heterogeneous dose-effect response into account. Dual planning provides support for the statistical outcome modelling which increases trial power even if the dose-response model is moderately misspecified. The outcome of a trial in the example studied would be a randomized measure of benefit per Gy ∆MLD with confidence interval.

**EP-1725**

Predictors of diarrhea after whole pelvis post-prostatectomy radiotherapy

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**Purpose or Objective:** Gastrointestinal (GI) toxicity is a side-effect induced by whole pelvis intensity modulated radiotherapy (WP-IMRT), affecting importantly patients' quality of life. The aim of this study was to identify predictors of diarrhea in a cohort of chemo-naïf patients treated with WP-IMRT after prostatectomy.

**Material and Methods:** The Inflammatory Bowel Disease questionnaire (IBDQ) was used to assess the degree of GI symptoms after WP-IMRT, investigating 4 distinct areas: bowel and systemic symptoms, emotional and social functions. This study focused on the most clinically relevant item 5 relative to the bowel domain, in order to evaluate the differences between patients with/without diarrhea toxicity. We used to select the most discriminative DVH parameters.

**Results:** No significant correlation emerged for sigmoid colon, then the analysis was focused on intestinal loops. Patients without basal score and with ∆IBDQs≤-3 were excluded from the analysis: 23/77 pts showed acute GI toxicity. At univariate analysis, volumes receiving 5 to 40 Gy (V5-V40) were correlated with ∆IBDQs≤-3 (p=0.03). Multivariate analysis confirmed a leading role of dosimetric variables, while no significant correlation for clinical parameters was found. Best cut-off values (assessed by ROC) discriminating patients with/without ∆IBDQs≤-3 were: V20=250cc, V30=150cc and V40=90cc. The overall incidence equal to 10% and 50% resulted for the group of patients with DVH parameters lower/higher than thresholds, respectively (p=0.0028, OR=4.9, AUC=0.68).

**Intestinal loops**

<table>
<thead>
<tr>
<th>Dose (Gy)</th>
<th>Average DVH-constraints</th>
<th>Average DVH-constraints</th>
</tr>
</thead>
<tbody>
<tr>
<td>V20 ≤ 250 cc</td>
<td></td>
<td></td>
</tr>
<tr>
<td>V30 ≤ 150 cc</td>
<td></td>
<td></td>
</tr>
<tr>
<td>V40 ≤ 90 cc</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** Low-medium IMRT doses to intestinal loops were correlated to diarrhea symptom at half/end of RT. This study proposed new dose volume constraints, that may be used to prevent much radiation-induced GI morbidity.

**EP-1726**

Biological modelling to identify proton therapy candidates in focal boosting of prostate tumours


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**Purpose or Objective:** MRI-based focal tumour boosting is currently under clinical investigation for prostate cancer patients, e.g. in the FLAME trial. These highly conformal, focal dose distributions can be difficult to achieve with photons, depending on the size and location of the boost volume (i.e. proximity to critical organs at risk). Selected patients might therefore be candidates for proton therapy. In previous work we have established an MRI-based tumour control probability (TCP) model. Combined with published rectum and bladder normal tissue complication probability (NTCP) models we have in this study explored the use of biological (TCP and NTCP) models to identify prostate cancer patients that might be suitable candidates for proton therapy if treated according to FLAME-like trial protocols.

**Material and Methods:** CT scans of seven patients from a prospective trial in our institution were used for planning. To obtain realistic boost geometries, MRI-based index tumours from a different cohort were used (matched on prostate volume), propagated with rigid registration on the prostate volume. VMAT plans (Eclipse, Varian Medical Systems) with and without a boost to the index lesion (95 Gy / 35 fx) were created; both plans delivered a conventional dose (77 Gy / 35
Patterns.

Focal boost cannot be achieved with state of the art photon-based method to identify prostate cancer patients where the focal boost; Table 1). These two patients had the index lesion that was closest to the bladder.

Results: The TCP increased from a median (range) of 0.45 (0.08-0.83) with the conventional approach to 1.0 (no range) with the focal boost. While there were only minor differences in the rectum NTCPs with vs. without the boost there were considerable differences in the NTCP for the bladder for two of the patients (more than a doubling of the NTCP with the boost; Table 1). These two patients had the index lesion that was closest to the bladder.

Table 1: NTCP values for each patient for rectum and bladder. First value is with boost, second value without boost.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Rectum</th>
<th>Bladder</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>With boost</td>
<td>Without boost</td>
</tr>
<tr>
<td>Patient 1</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Patient 2</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Patient 3</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Patient 4</td>
<td>1%</td>
<td>2%</td>
</tr>
<tr>
<td>Patient 5</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>Patient 6</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Patient 7</td>
<td>2%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Conclusion: We have established a biological modelling based method to identify prostate cancer patients where the focal boost cannot be achieved with state of the art photon-based treatment without a considerable increase in the NTCPs. Further work will consider the feasibility of proton planning, given both inter- and intra-fractional organ motion patterns.

Figure 1: The upper part of the figure shows the dose distribution for one patient with the tumour boost (the index lesion is the peanut shaped delineation made from the PTV of the prostate). The dose color wash range is between 74 Gy and the max dose, which is 154 Gy. The lower part of the figure shows the same view of the same patient without the boost arm, but conventional treatment. The dose color wash range is between 74 Gy and the max dose, which is 81 Gy.

EP-1727
A decision support system for localised prostate cancer treated by external beam radiation therapy
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Purpose or Objective: This study presents a universally applicable decision support system (DSS), with respect to the prediction of five-year biological no evidence of disease (SybNED) for localised prostate cancer (PCa) patients treated by external beam radiation therapy (EBRT).

Material and Methods: To develop a DSS this study utilised the traditional approach of model training based upon meta-analysis data (MAAD: n=5218) from the literature with model validation based upon routine clinical care data (CCD: n=827) from clinics with a rapid learning healthcare (RLHC) environment. The following standard clinical features for PCa patients were investigated to train and validate a tumour control probability model (TCP) and a predictive machine learning model (PML): primary tumour stage (T), lymph node stage (N), metastasis stage (M), prostate specific antigen (PSA), Gleason score (GS), clinical-target-volume (CTV), total dose (D), and fractional dose (d). These features were selected as they are typically known within all clinics treating PCa patients, thus maximising the generalisability of the DSS.

Results: The DSS is comprised of two distinct models. The TCP model was found to be well calibrated with poor discriminative ability. Training resulted in an adjusted weighted R2 value of 0.76, a weighted mean absolute residual (wMAR) of 4.7% and an area under the curve (AUC) of 0.67 [0.65, 0.69]. Validation resulted in an adjusted weighted R2 value of 0.51, a wMAR of 2.0% and an AUC of 0.57 [0.51, 0.63]. Contrastingly, the PML model was found to be poorly calibrated with good discriminative ability. Training resulted in an adjusted weighted R2 value of 0.27, a wMAR of 8.3% and an AUC of 0.66 [0.64, 0.68]. Validation resulted in an adjusted weighted R2 value of 0.90, a wMAR of 16.2% and an AUC of 0.61 [0.56, 0.65]. Subset analysis shows that the DSS performs best in high-risk PCa patients with validation resulting in an AUC of 0.66 [0.60, 0.72] with a wMAR of 1.0%.

Conclusion: A DSS developed with MAD has been validated in CCD extracted using RLHC infrastructure. The DSS uses standard clinical features to estimate with good accuracy (wMAR < 4.7%) and reasonable fidelity (AUC > 0.61) the SybNED rate and classification, respectively, of PCa patients. The performance of the DSS in the validation high-risk PCa cohort (wMAR = 1%) and patients (AUC = 0.66) for whom therapy could be potentially adapted or individualised based on the DSS has clinical relevance and should be prospectively validated.

EP-1728
Dose individualisation through biologically-based treatment planning for prostate cancer patients
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Purpose or Objective: The use of biological information on tumour control and normal-tissue complications for treatment plan optimisation can be used for individualising the dose prescription. For patients with prostate cancer, moreover, the tumour localisation by means of MR-images facilitates the use of such information for a simultaneous dose escalation in the so-called dominant intraprostatic lesions (DIL), thus further improving the treatment outcomes. However, a correct modelling of the tumour-control