Conclusion: Treatment intensification in NSCLC via targeted dose escalation with modern delivery techniques offers the potential for a significant increase in tumour control probability without a clinically significant increase in predicted OAR toxicity.

EP-1713
Dose-volume analysis of genitourinary toxicity in 3-D conformal radiotherapy for prostate cancer
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Purpose or Objective: We investigated the associations between acute and late genitourinary (grade ≥ 2) toxicity and clinical and dosimetric parameters in three-dimensional conformal radiotherapy for localized prostate cancer in order to carry out a dose-volume response evaluation. A dose-volume parameters analysis of the bladder of patients subjected to prostate cancer radiotherapy was reported.

Material and Methods: We considered 86 patients consecutively treated with high dose conformal image guided radiation therapy for localized prostate cancer. For the purpose of our analysis, we defined two bladder volumes: “whole bladder”, i.e. the bladder in its entirely as a solid organ, and “inferior bladder”, corresponding to the only distal part of the bladder. We carried out an univariate analysis between acute and late genitourinary toxicity and clinical parameters (age, “whole bladder” and “inferior bladder” volumes, smoking status, pre-radiotherapy urinary symptoms, hormonal therapy). We used the point biserial correlation coefficient to correlate dose-volume parameters (Vx) and genitourinary (grade ≥ 2) toxicity. Finally, a fitting of the normal tissue complication probability (NTCP) cut-off volume model with toxicity data was performed.

Results: Mean follow-up was 51.9 months (range: 41.9-75.4 months). In 60 patients we observed an acute genitourinary toxicity (grade ≥2), while a late genitourinary toxicity (grade ≥2) was recorded in 6 patients. At univariate analysis, we found a correlation between acute genitourinary toxicity and smoking status (P < 0.001). Statistically significant associations (P < 0.05) between late genitourinary toxicity and Vx dose levels were calculated from 77 Gy and 77.5 Gy, for the “whole bladder” and the “inferior bladder”, respectively. For acute toxicity, we found a statistically significant correlation with the dose of 80 Gy (P < 0.05), for both “whole bladder” and “inferior bladder”. From the NTCP cut-off volume model we detected a bladder volume of 6 cc as the cut-off volume corresponding to a late genitourinary cut-off volume model we detected a bladder volume of 6 cc significant correlation with the dose of 80 Gy (P < 0.05), for respectively. For acute toxicity, we found a statistically significant correlation between acute and late genitourinary toxicity and smoking status (P < 0.001). Statistically significant associations (P < 0.05) between late genitourinary toxicity and Vx dose levels were calculated from 77 Gy and 77.5 Gy, for the “whole bladder” and the “inferior bladder”, respectively. For acute toxicity, we found a statistically significant correlation with the dose of 80 Gy (P < 0.05), for both “whole bladder” and “inferior bladder”.

Conclusions: Genitourinary toxicity seems to be correlated with bladder maximal doses, quantified as hotspots.

EP-1714
Hyper- versus hypofractionated radiotherapy in a radioresistant head and neck cancer model
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Purpose or Objective: Cancer stem cells (CSCs) and hypoxia are known contributors of tumour resistance in radiotherapy. These parameters influence the radiotherapy schedule for optimal tumour control. Since hypofractionation is becoming increasingly popular among solid tumours, our aim is to evaluate the efficacy of hypo- versus hyperfractionated radiotherapy (RT) on hypoxic head and neck cancer (HNC).

Material and Methods: An in silico HNC was developed starting from a CSC. To grow a tumour with biologically valid parameters, the CSC generates all heterogeneous lineages of a tumour, with a probability of CSC symmetrical division 1.9%, mean cell cycle time 33h and volume doubling time 52 days. Pre-treatment CSC percentage is 5.9%. Four different fractionation schedules have been simulated as shown in Table 1. Hypoxic tumours with partial oxygen tension values ranging from 3 to 9 mmHg have been treated and tumour control assessed.

Table 1. Dose fractionation schedules simulated in current study

<table>
<thead>
<tr>
<th>Radiotherapy schedule</th>
<th>Fractionation pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional RT</td>
<td>2 Gy/day; 5 days a week</td>
</tr>
<tr>
<td>Hypofractionated 4d RT</td>
<td>2.2 Gy/day; 5 days a week; 6 weeks</td>
</tr>
<tr>
<td>Hypofractionated 6d RT</td>
<td>2.2 Gy/day; 6 days a week; 5 weeks</td>
</tr>
<tr>
<td>Hypofractionated RT</td>
<td>2.4 Gy/2 times daily; 5 days a week; 7 weeks</td>
</tr>
</tbody>
</table>

Results: Treatment resistance is determined by the interplay between CSCs and hypoxia. While the modelled conventional and hypofractionated RT schedules are biologically equivalent, hypofractionation is more efficient on CSC kill than conventional treatment. However, for moderately hypoxic tumours (6 mmHg partial oxygen tension) (see figure 1) only hyperfractionated RT offers full control on CSC population within the clinically required treatment time. This observation might be explained by the advantage of two fractions a day through (i) overcoming tumour repopulation between consecutive doses, (ii) redistribution of surviving cells along the cycle; (iii) better reoxygation. For each decrease in mmHg the number of fractions needed for tumour control increases exponentially. This behaviour is also influenced by the percentage of CSC, which changes during radiotherapy. Thus a tumour with a mean oxygen tension below 6 mmHg and a pre-treatment CSC population of 5.9% needs a greater than 84Gy dose (overall dose given via hyperfractionated RT) or the addition of adjuvant therapies in order to be eradicated.

Conclusion: Hypoxic HNC are better controlled by hyperfractionated than by hypofractionated RT. However, oxic and mildly hypoxic tumours could benefit from hypofractionation, which reduces overall treatment time and normal tissue effects. The interplay between CSCs and hypoxia dictates the RT treatment strategy for optimal tumour control.

EP-1715
A Neural Network predictions and follow-up toxicity correlation to validate re-planning during RT
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Purpose or Objective: Based on the premise that the effective radiation dose deposited at the tumour site is not necessarily the dose prescribed to that site, we developed a neural network prediction model to predict OAR toxicity using pre-treatment clinical and dosimetric parameters as inputs, and a follow-up toxicity cohort as the output. This model was then used to predict toxicity for the current cohort.

Results: The neural network model showed a good correlation with the follow-up toxicity cohort, with an average absolute prediction error (APE) of 2.1% and a maximum absolute prediction error of 7.2%. The model was then used to predict toxicity for the current cohort, showing a good correlation with the predicted toxicity, with an APE of 2.3% and a maximum APE of 5.1%.

Conclusion: The neural network model shows promise as a tool for predicting OAR toxicity in radiation therapy, and could be used to improve the planning process and reduce treatment time for patients.