EP-1711
To revise helical irradiation of the total skin HITS as completed-HITS in cutaneous lymphoma patient
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Purpose or Objective: To modify helical irradiation of the total skin (HITS) technique as the completed-HITS (CHITS) with face covering and the bone marrow dose declined according to the relapse pattern and hematologic toxicities of cutaneous lymphoma patient.

Material and Methods: A 36-year-old woman was diagnosed as therapy-refractory cutaneous CD4+ T-cell lymphoma, T3N0M0B0, stage IIIB. HITS with face sparing using 30 Gy in 40 fractions, 4 times per week was prescribed in March, 2012. The adverse effects included leukopenia. One year later, the new patches were noted in right eyebrow and lower eyelid which was spared. According to the relapse pattern and hematologic toxicities, HITS was revised to improve the plan results as CHITS. First, the clinical target volume (CTV) was increasing the face targeting to be really whole skin irradiated. Second, the planning target volume (PTV) were separated into head, chest, abdomen and pelvis with upper thigh to maintaining the appropriate PTV coverage and the margin for PTV was reduced from 5.0 mm to 3.0 mm according to the previous daily image-guided data. Third, the central cord complete block (CCCB) was designed from head to thigh but not from head to abdomen only. The CCCB distance away from PTV was changed from 2.5 cm to 2.2 cm to reduce the internal organs and bone marrow dose. Additionally, the iliac bone, cervical, thoracic, lumbar spine, femoral head and pelvic bone were contoured to be references to limit the marrow dose. The uniformity index (UI), conformity index (CI), dose of organs at risk were used to evaluate the plans. For reducing the toxicity of normal organs, we also performed low-dose CHITS of 12 Gy in 12 fractions.

Results: The UI for head, chest, abdomen and pelvis of CHITS were 1.16, 1.12, 1.08 and 1.12, respectively. For the low-dose CHITS, the UI was also similar to CHITS. The conformity of CHITS was similar to HITS (1.40 versus 1.37). The mean dose of heart, whole lung, right parotid gland, left parotid gland, liver, right kidney, left kidney, intestine, bladder, rectum, uterus with ovary, and cervix with vagina were reduced in 15.1% to 45.0%. The mean dose of cervical spine, thoracic spine, lumbar spine, right iliac bone, left iliac bone, sacrum, right lower pelvic bone, left lower pelvic bone, right femur, left femur were reduced in 21.6% to 63.8%. For the low-dose CHITS, the normal organ dose were reduced in 47% to 88% due to low dose treatment.

Conclusion: The modifications of adding face skin irradiation, reduced PTV margin, the distance away from PTV from CCCB and virtual structure constraints enabled the CHITS technique reduced doses of normal organs and bone marrow successfully with keep of uniformity and conformity as HITS technique. The low-dose CHITS had the similar results in target uniformity and conformity and much lower normal organ dose compared to HITS technique.

EP-1712
Increased tumour control probability (TCP) with inhomogeneous dose escalated distributions in NSCLC
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Purpose or Objective: The theoretical benefit of dose escalation in NSCLC has been shown by Fenwick whilst others have demonstrated a clinical dose response relationship (Partridge, Rengan). Additionally, inhomogeneous dose distributions have been suggested as a method for increasing the absolute dose to the target within normal tissue constraints (Warren). The aim of this planning study was to combine these concepts and explore the potential tumour control probability (TCP) benefit that an inhomogeneous plan targeting dose escalation to the IGTV could deliver whilst respecting normal tissue tolerances.

Material and Methods: Between January 2014 and April 2015 20 patients with non-small cell lung cancer (NSCLC) underwent 4D-planning CT with motion tracking via the RPM system (Varian Medical Systems, Palo Alto, California) for definitive (chemo)radiotherapy at our institution. The 4DCT scan was binned into 10 phases and the MIP and AVIP datasets were generated. The iGTVsum was the sum of three datasets (0%, 50% and MIP). An iGTVM of 6mm (scc) or 8mm (adenocarcinoma) was used with a further 5mm to the PTV. OARS were contoured on the AVIP CT set, including: combined lung; spinal cord; oesophagus and heart.

Results: There is a significant (p < 0.05) difference in TCP for all escalated plans, ranging from 79.8% for the 65Gy boost to 94.9% for the 80Gy boost, in comparison to 63.1% for the homogeneous RapidArc plan. There is a significant difference between the MLD for the various escalated plans (Table 1); however, this difference is not clinically significant given that tolerance for MLD is in the 17-20Gy region. Similarly, the predicted NTCP for the lung for the dose escalated plans ranged from 6.2-7.1%. In terms of the V20Gy the only significant difference was between the 3D plan and all the RapidArc plans (Table 1).

The only significant mean osteophagal difference was between the 3D plan (20.6Gy) and all the escalated plans (17.7-18Gy); however, dose to 1cc of the oesophagus was significantly higher for the 80Gy and 3D plans. All spine, lung, and heart doses were below tolerance for the escalated plans.
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 toxicity (grade ≥ 2) 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 toxicity of 50% at doses ≥77 Gy.

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

EP-1714
Hyper- versus hypofractionated radiotherapy in a radioreistant 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>
<thead>
<tr>
<th>Radiotherapy schedule</th>
<th>Fractionation pattern</th>
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<tbody>
<tr>
<td>Conventional RT</td>
<td>2 Gy/day; 5 days a week; 7 weeks</td>
</tr>
<tr>
<td>Hypofractionated 4d RT</td>
<td>2.2 Gy/day; 5 days a week; 6 weeks</td>
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<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>2.2 Gy/twice daily; 5 days a week; 7 weeks</td>
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</tbody>
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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 the fractions a day through (i) overcoming tumour repopulation between consecutive doses, (ii) redistribution of surviving cells along the cycle; (iii) better reoxygenation. 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.

Figure 1. Radiotherapy schedules for hypoxic HNC with 6 mmHg mean partial oxygen tension.

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: To evaluate the efficacy of hypo- versus hyperfractionated radiotherapy (RT) on hypoxic head and neck cancer (HNC).