

Fig 1. FF-ANN scheme.

**Results:** An inverse correlation of the radio-sensitivity parameter assessed by the model was found with respect the  $dR2^*$  ( $-0.65$ ) for the Oxy group. A further subdivision according to positive and negative values of  $dR2^*$  showed a larger average radio-sensitivity for the Oxy rats with  $<0$  and a significant difference in the two distributions according to the Wilcoxon-Mann-Whitney test ( $p < 0.05$ ). Finally, the Pearson correlation coefficient ( $R^2 > 0.9$ ) revealed a strong agreement of the FF-ANN output with the target radio-sensitivity.

**Conclusion:** These preliminary findings support the hypothesis that the change in the  $R2^*$  can be related to tumor oxygenation and, consequently, to its radio-sensitivity. In particular, the sign of the tendency is in accordance with the fact that an oxygenation increase reduces the tumor relaxation rate as reported in the literature. Moreover, the different distributions of  $\alpha$ , outlined in the Oxy subgroups according to the  $dR2^*$ , suggest that some subjects would benefit from oxygen inhalation more than others, reasonably due to their initial vascularization. Finally, the performance of the FF-ANN is promising, although it would require a larger dataset to validate its prediction ability.

#### EP-1719

**Radiobiology based head & neck cancer protocol (FAMOSO) combining accelerated RT and EGFR inhibitor**

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**Purpose or Objective:** Administration of monoclonal antibody Epidermal Growth Factor Receptor (MoAb-EGFR) inhibitor every week during Radiotherapy (RT) of head and neck cancer (HNC) has shown improved outcomes as compared to RT alone in terms of locoregional disease control, progression free and overall survival, thanks to its radiosensitizing effect. MoAb-EGFR concentration varies day by day after injection, and radiosensitizing effect accordingly. A radiobiological (RB) model accounting for this variation (Pedicini, et al. Radiat Oncol. 2012;7:143) can be applied to shorten the treatment by optimizing daily RT dose, still maintaining unchanged the biological effect on the

tumour (in terms of surviving cells) as compared to standard RT (7 weeks, PTV1: GTV, 70Gy; PTV2 = GTV+margin, 63Gy; PTV3: lymph nodes: 58.1Gy) and potentially reducing healthy tissue toxicity. In this study, such RB model was adopted in the clinical protocol FAMOSO (Frazionamento Accelerato MOdulato in SIB-IMRT dei tumori testa-collo) for the treatment of HNC tumours with simultaneous integrated boost (SIB), aiming to test the feasibility of accelerated modulated fractioning and to assess toxicity and response rate.

**Material and Methods:** From literature data, showing that higher concentrations of MoAb-EGFR correspond to steeper tumor cell survival curves, radiobiological parameters were derived and included in the RB model to obtain the daily dose to be delivered to each target volume. To date, 2 of the 10 expected pts (pt1: cT4cN1 oropharyngeal; pt2: cT2 cN3 supraglottic squamous cell carcinoma) have been recruited and treated with SIB-IMRT with a curative intent.

**Results:** The RB model suggested a 6 week treatment with daily increasing dose/fractions as follows: PTV1: 1.70, 1.95, 2.15, 2.30, 2.35Gy; PTV2: 1.50, 1.75, 1.95, 2.05, 2.10Gy; PTV3: 1.40, 1.60, 1.80, 1.90, 1.95Gy. Both pts recruited in the FAMOSO protocol concluded the radiation treatment: pt1 with no change of the planned schedule; pt2 with interruption of MoAb-EGFR after the 5th administration and, consequently, the last 10 RT fractions of RT were administered with standard fractionation. The total dose to the PTV1 were 62.7 and 61.8 Gy, respectively. Maximum acute skin and mucosal toxicity was G3. With a follow up of 6 and 2 months, a partial response was obtained for pt1, while pt2 is still under evaluation.

**Conclusion:** New treatment strategies, even accelerated, are feasible when combining RT with radiosensitizing drugs. The RB model is adequate to set up the treatment provided radiobiological parameters are available from clinical data. The preliminary clinical data of the protocol FAMOSO give encouraging results, suggesting that the treatment schedule is feasible with acceptable acute toxicity. Longer follow up is needed to confirm toxicity findings and assess response rate, and of course more patients have to be studied.

#### EP-1720

**Impact of contouring variability on tumour control and normal tissue toxicity in liver SBRT**

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**Purpose or Objective:** Variability in the contouring of gross tumour and the derived planning target volumes (PTVs) between clinicians is well-known in radiotherapy. This study aims to quantify the impact of variability in contouring in terms of tumour control and normal tissue toxicity in Liver SBRT.

**Material and Methods:** The National Radiotherapy Trials Quality Assurance (RTTQA) Group planning benchmark case for the ABC07 Trial was used (addition of stereotactic body radiotherapy to systemic chemotherapy in locally advanced biliary tract cancers; CRUK A18752, sponsor University College London). 12 centers performed contouring independently using radiotherapy trial protocol as per RTTQA pre-trial QA process. Each centre applied margins to derive PTV as per local practice. A standardised Volumetric Modulated Arc Therapy (VMAT) plan was produced based on gold standard contours and applied to all 12 sets of submitted contours aiming to deliver 50Gy in 5 fractions. However, due to large GTV this was unavoidably de-escalated to 40Gy to meet trial mandatory mean non-GTV Liver constraint. Tumour control was assessed through biologically effective dose (BED) to 98, 95 and 90% of the gold standard PTV. 65Gy BED, although disappointingly low for SBRT, was considered

as a cut off for acceptable therapeutic intent. NTCP modeling of radiation induced Liver disease was also performed.

**Results:** Non-GTV Liver mean dose ranged from 13.1 to 17.0Gy, breaching mandatory trial constraint of <15.2Gy in three cases. NTCP ranged from 0.0 to 0.3 assuming an alpha/beta of 1.0 for normal Liver and negligible assuming alpha/beta of 2.0 or more. At D98%, four sets of contours did not achieve 65Gy BED to gold standard PTV, two sets failing to reach 65Gy BED at D90%.

**Conclusion:** Significant variability exists in contours drawn by different centers/clinicians in the setting of pre-trial QA to the extent where 10% or more of the PTV receives a BED insufficient for local control in a proportion of cases and NTCP is significantly affected. Given this variability, the pre-trial and on-trial RTTQA process is essential if the effect of contour variability on tumour control rates and treatment toxicity is to be mitigated.

#### EP-1721

Feature extraction from duodenal dose surface maps to predict toxicity in pancreatic chemoradiation

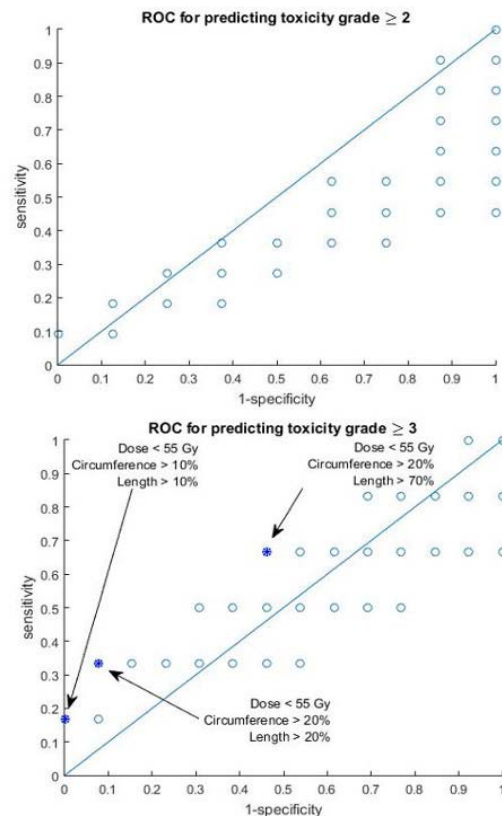
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**Purpose or Objective:** To use spatial features from dose surface maps of the duodenum to predict acute duodenal related toxicity in pancreatic chemoradiation.

**Material and Methods:** Dose surface maps were produced for the duodenum describing the spatial surface dose distribution. Traditional metrics were extracted including mean and max dose, surface area receiving 25, 35, 45 and 55 Gy as absolute and fraction of the surface. Spatial metrics extracted include the length of the duodenum which received less than 25, 35, 45 and 55 Gy to at least 10-90% of the circumference (in 10% intervals). Different thresholds for the length of the duodenum achieving these constraints were tested in order to find the best predictor of toxicity. Toxicity results from 19 patients from the ARCII clinical trial (EudraCT: 2008-006302-42) were used as a proof of concept. 6 and 11 patients had grade (Gr) 1 and Gr ≥2 toxicity respectively.

**Results:** The best predictors for patients with grade (Gr) ≥3 toxicity were at higher doses of 55 Gy. While restricting the dose < 55 Gy to at least 10% of the circumference for at least 10% of the length of the duodenum, or at least 20% of the circumference for at least 20% of the length accurately predicted toxicity for 74% of the patients studied, this only had a sensitivity of 17% and 33% respectively (specificity of 100% and 92%). Figure 1 indicates a better predictor may be restricting dose < 55 Gy to at least 20% of the circumference for at least 70% of the length which, although only accurately predicts toxicity for 58% of the patients, has a sensitivity and specificity of 67% and 54%. It was found that the relative percentage of the circumference spared was a better predictor than absolute circumferential length spared. However, similarly to the spatial metrics, predictions of patients with at least Gr 3 toxicity was seen in the higher dose regions such as mean dose of 60 Gy, maximum dose to a pixel of 62 Gy and when 70% of the surface area receives 55 Gy. Gr 2 toxicity could not be predicted.



**Figure 1:** ROCs for grade ≥ 3 and grade ≥ 2 toxicity. Each point represents a different dose-surface feature and threshold that was tested.

**Conclusion:** In this small sample we have shown that spatial features can be extracted from dose surface maps to aid toxicity prediction, and that high doses to the duodenum appear to be correlated with Gr 3 toxicity. An improved understanding of how these spatial features correlate to toxicity can improve traditional constraints on the duodenum. Further work is required to build a more complete picture of this result, and the analysis will now be extended to a larger patient cohort.

#### EP-1722

Simulation of the radiation response of a hypoxic prostate tumor in the rat

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**Purpose or Objective:** In a previous work a model which simulates the radiation response of hypoxic tumors was developed. The task of this work is to validate the model by using preclinical experimental dose response data of rat prostate tumors for single and multiple irradiations.

**Material and Methods:** The model is voxel-based and simulates the spatio-temporal behavior of tumors considering six radio-biological processes. Important input data are the oxygenation levels of each tumor subvolume at the time of irradiation, which are given as pre-calculated oxygen frequency histograms. The experimental data for validation include growth curves, dose response curves and TCD50s for 1, 2 and 6-fraction (Fx) experiments. A very high  $\alpha/\beta$  value of  $84.7 \pm 13.8$  Gy was determined. A strategy of adjustment was