severity. A modified normal tissue complication probability (NTCP) model has been investigated to describe AMT data in radiotherapy regimes, both conventional and altered in dose and overall treatment time (OTT). We tested the hypothesis that such a model can also be applied to identify intolerable treatment and predict AMT and late toxicity. NTCP model has been compared with other published predictive models to identify schedules that are either tolerable or not. The Area Under Curve (AUC) was calculated for all models assuming treatment tolerance as the gold standard. NTCP model for late effect was also calculated. The correlation between AMT/late toxicity and the predicted toxicity rate was assessed by a Pearson correlation test.

Results: The AMT NTCP model was able to distinguish between acceptable and intolerable schedules among the data available for the study (AUC=0.84, 95%CI:0.75-0.92). In the equivalent dose at 2Gy/fraction (EQD2) versus OTT space, the proposed model shows a similar trend to that of models proposed by other Authors, but was superior in detecting some intolerable schedules. Moreover, it was able to predict the incidence of ≥G3 AMT. A correlation between the modified late NTCP model and ≥G3 late toxicity has been found as trend (p=0.07).

Conclusions: The proposed acute NTCP model is able to predict ≥G3 AMT after HN cancer radiotherapy and could be useful for designing altered/ hypofractionated schedules in order to reduce the incidence of AMT. Late NTCP model was able to predict late toxicity but requires further improvements to increase the predictive power.

PD-0495 Prediction of rectal bleeding in prostate cancer radiotherapy: blind source separation approaches

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Purpose/Objective: Current models for toxicity prediction in prostate cancer radiotherapy are based on the dose-volume histograms which lack of spatial accuracy. The goal is to propose new methods able to predict late rectal bleeding following high-dose prostate cancer radiotherapy. The aim is to fully exploit the tri-dimensional planning Dose Distribution (pDD) to study the correlation with rectal toxicity.

Materials and Methods: A total of 63 patients having received a dose of 80Gy in the prostate by IMRT have been included in the study. Twelve of them presented rectal bleeding (≥ grade 1) at two years. Only the 3D pDD within the rectum was analysed. Our work has been divided in different steps:

1. Registration
Individuals Computed Tomography (CT) from the planning and pDD were elastically registered using the demons algorithm to a single coordinate system by combining the CTs and organs delineations.

2. Training step
The training step consisted in learning from the data two vector subspaces spanning the 3D pDD of patients with toxicity and those of patients without toxicity, respectively. The different methods used to compute this subspaces have different constraints: orthogonality for Principal Component Analysis (PCA), mutual statistical independence for Independent Component Analysis (ICA).

3. Validation
A new patient was classified by evaluating its distances to this two subspaces. We computed the euclidean distance between this patient and it orthogonal projector in the two subspaces. Eventually, this patient is classified as toxic if the distance (dt) from the subspace representing toxic patients is less than the distance from the other subspace (dnt).

4. Classification
A leave-one-out cross validation and statistical measures - sensitivity and specificity - were used to evaluate the classification performance. The sensitivity assesses the percentage of toxic patients who are correctly identified as having toxicity. The specificity assesses the percentage of patients who are correctly identified as not having toxicity.

Results: PCA method classified with 1 sensitivity and 0.76 specificity. ICA method allowed to classify perfectly rectal bleeding. Figure 1 shows the distance representation of each patient for ICA method. Two significant clusters were identified.

Conclusions: Our statistical approaches conjointly exploit 3D spatial patterns of dose. pDD and late rectal bleeding appear to be correlated. However, larger data base of patients will enable to use more robust classifiers. Our results will be compared with those obtained with existing models (i.e. NTCP).

PD-0496 Multi-centric learning with a federated IT infrastructure: application to 2-year lung-cancer survival prediction

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Purpose/Objective: To validate the hypothesis that multi-centric learning produces better models than models built on data from individual centers only.

Materials and Methods: We created an IT multi-centric network, which connects the databases of 5 clinical centers across 3 European countries. The network is a federated database where certain rules apply to ensure that data privacy is preserved, data never leaves the boundaries of its institution of origin, and secure traffic through firewalls is achieved. We then tested whether learning from federated data via the network gives advantage over single-center learning in the following way. A dataset 322 non-operable and non-metastatic non-small cell lung cancer patients treated with definitive (chemo)radiotherapy was distributed with unequal proportions across 5 centers. A model was built for each center using only the locally available data. A distributed learning model was deployed in the IT network which has a read-only, no-copy access to local data. The chosen model was the Support Vector Machines (SVM) classifier, solved with the Alternating Direction Method of Multipliers method, which enables learning from data stored in different locations in a distributed way. The biggest advantage of this method is that the model learnt from scattered data across centers is exactly the same as if the data was centrally available.

Results: The 5 centers had the following number of lung cancer patients available in the infrastructure: 186, 52, 45, 7 and 32, respectively. The predicted variable was 2-year survival, with predictor variables gender, World Health Organization performance status, forced expiratory volume in 1 second, number of positive lymph node stations, gross tumor volume and biologically-equivalent (at 2 Gray) total dose. No survival data was censored. We used the data at center 1 as an external validation set within the network. Model performance was evaluated using the area under the receiver operating characteristic curve (AUC). Models built separately on centers 2 to 5 had AUCs of 0.75, 0.68, 0.61 and 0.72 when validated on center 1. The AUC values fluctuate substantially, which reflects to a high degree the current model-learning reality and leaves open the question of how a combined-data model would perform. We can answer this question using the network: the distributed SVM model built on all data from centers 2 to 5 without any data leaving its origin had an AUC of 0.77 on center 1 (see Figure 1).
Identification of residual cohort

Use of STAT in prostate cancer: correlation with risk factors and specific tumorigenic stem cells during the continuing radiotherapy. Repopulation that suggests the involvement of subpopulations of off time for accelerated repopulation and a surprisingly fast estimated cell doubling time value for parameters for prostate cancer. With our analysis we confirm a low required to offset the repopulation occurring in one day (D_prolif) compared to that reported in literature. This corresponds to the dose reported to offset the repopulation occurring in one day (D_prolif) of 5.1 days (4.2-7.2) 95%, very low if compared to that reported in literature. This corresponds to the dose required to offset the repopulation occurring in one day (D_prolif) of 0.32-0.68 GY. However, a long kick-off time of 31 days (22-41) from the start of radiotherapy was found.

Conclusions: The access to federated multi-centric data enables creating more reliable and more robust models than those based on single-center data. The infrastructure has inherent external validation capabilities that are available at virtually no extra cost of time. There is therefore an enormous potential of using such kind of infrastructure for learning more accurate and reliable medical prediction models in the future.

PD-0497

Estimation of a self consistent set of radiobiological parameters of prostate cancer

Purpose/Objective: To determine a self consistent set of radiobiological parameters in prostate cancer. Materials and Methods: A method to estimate intrinsic radiosensitivity (α), fractionation sensitivity (α/β), repopulation doubling time (T_d), number of clonogens (M) and kick-off time for accelerated repopulation (T_k) of prostate cancer, has been developed. Based on the generalized linear quadratic model (LQ) and without assuming the iso-effective hypothesis, the potential applications of the method were investigated using the clinical outcome of the biochemical relapse free survival (bRFS) recently reviewed in literature. The strength and limitation of the method, regarding the fitted parameters and 95% confidence intervals, are also discussed. Results: Our best estimate of α/β is 2.96 Gy (2.41-3.35)_{95%}. The correspondant α values is 0.16 Gy^{-1} (0.14-0.18)_{95%}, which is compatible with a realistic number of clonogens: 6.5-10^5 (1.5-10^5-2.1-10^5)_{95%}. The estimated cell doubling time T_d is 5.1 days (4.2-7.2)_{95%}, very low if compared to that reported in literature. This corresponds to the dose required to offset the repopulation occurring in one day (D_prolif) of 0.32-0.68 GY. However, a long kick-off time of 31 days (22-41) from the start of radiotherapy was found.

Conclusions: The proposed analytical/graphical method has allowed to fit clinical data providing a self-consistent set of radiobiological parameters for prostate cancer. With our analysis we confirm a low value for α/β with a correspondingly high value of intrinsic radiosensitivity, a realistic average number of clonogens, a long kick-off time for accelerated repopulation and a surprisingly fast repopulation that suggests the involvement of subpopulations of specifically tumorigenic stem cells during the continuing radiotherapy.

PD-0498

Use of STAT in prostate cancer: correlation with risk factors and identification of residual cohort

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