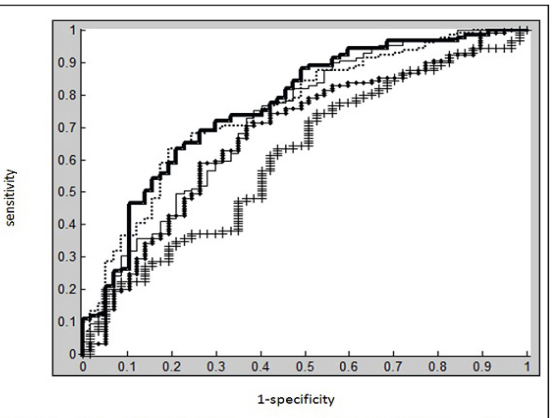

Figure 1. Model performance (AUCs) when using separate as well as "combined" data from centers 2-5 and evaluated on center 1. The AUCs are: 0.75 for center 2 (dotted), 0.68 for center 3 (solid with circles), 0.61 for center 4 (crosses), 0.72 for center 5 (thin solid) and 0.77 for "combined-data" model from centers 2-5 (thick solid). The data are never actually combined as they do not leave the borders of the institution of origin.

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

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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 (N) 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 $(2.41\text{-}3.53)_{95\%}$. The correspondent α valueis 0.16 Gy^{-1} $(0.14\text{-}0.18)_{95\%}$ which is compatible with a realistic number of clonogens: $6.5\cdot10^6$ $(1.5\cdot10^6\text{-}2.1\cdot10^7)_{95\%}$. The estimated cell doubling time Td is 5.1 days $(4.2\text{-}7.2)_{95\%}$, 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 0.51 Gy/day $(0.32\text{-}0.68)_{95\%}$. However, a long kick-off time T_k of 31 days $(22\text{-}41)_{95\%}$ 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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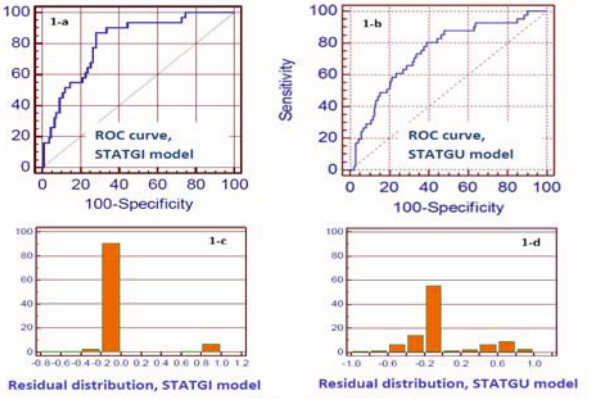
Purpose/Objective: Standardized Total Average Toxicity (STAT) score was proposed by Barnett (IJROBP11) as a global score which may be used to:
(a) facilitate the analysis of overall radiation (RT) toxicity (tox)
(b) pool data from multiple trials (in order to increase statistical power)
(c) select patients (pts) to be included in studies of possible genetic determinants of RT tox.
In the same paper application of STAT to 2 cohorts of breast cancer pts was presented.
We here evaluate application of STAT to 2 prostate cancer populations (A and B), with the aim of verifying that STAT keeps all known correlations of single tox endpoints with clinical/dosimetric risk factors and to select possible radiosensitive pts
Materials and Methods: Population A (646 pts, doses 70-80Gy,1.8-2Gy/fr) was included in a prospective trial on rectal tox (recorded by questionnaires).
Population B (179 pts, doses 60-80Gy,1.8-2.65Gy/fr) was included in a prospective trial on genito-urinary tox (measured by IPSS). STAT calculation was made following definition by Barnett. Key point is that STAT defines whether a pt's global tox is high or low relative to the distribution of the global tox of other pts. STAT measures the distance between the single pt and the average of all considered pts in terms of standard deviations.
For population A, 2 STATs were considered: baseline STAT (BSTAT) and late (3yrs follow-up) STAT (STATGI). For population B, only acute tox was available and acute STAT (STATGU) was calculated. We considered pts with STATGI/STATGU>0.8 as exhibiting high tox with respect to the whole cohort and clinical/dosimetric predictors of STATGI/STATGU>0.8 were determined through multivariable logistic analysis. Analysis of residuals was used to individuate the radiosensitive cohorts
Results: STATGI>0.8 (43/646pts) was predicted by: BSTAT (continuous variable (cv), OR=2, p=0.04), previous diseases of the colon (OR=3, p=0.02), the % volume of rectum receiving more than 40Gy (V40Gy, cv, OR=1.02, p=0.08) and V75Gy (cv, OR=1.05, p=0.03). Overall p=0.0006, AUC 0.74.
STATGU>0.8 (39/179pts) was predictedby: pre-RT IPSS (cv, OR=1.14, p=0.0008), Body Max Index (cv, OR=0.94, p=0.2), clinical T3 stage (OR=2, p=0.1), absolute bladder surface receiving ≥8.5 Gy/week (cv, OR=1.014, p=0.03) and absolute bladder surface receiving ≥12.5 Gy/week (cv, OR=1.035, p=0.06). Overall p<0.0001, AUC 0.81.
From analysis of residuals, 14 and 11 pts emerged as possible radiosensitive pts (with high STAT which is not predicted from model) for STATGI and STATGU, respectively.



ROC curves for STATGI (1-a) and STATGU (1-b) models
and distributions of residuals (1-c STATGI model and 1-d STATGU model)

Conclusions: Correlation between high STATGI/STATGU and clinical/dosimetric risk factors confirmed previously results found in the 2 populations for the single tox endpoints.
This global approach allows objective identification of pts whose tox are not explained by the global model and who may be included in studies of possible genetic determinants of RT tox