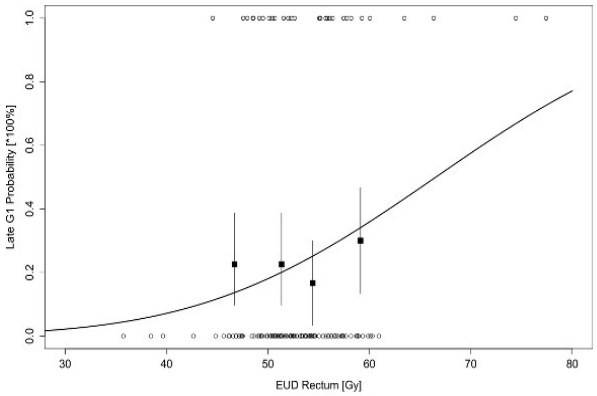
treatment on cancer and healthy cells, and these effects are generally characterized by tumor control probability (TCP) and normal tissue complication probability (NTCP). Nowadays, many attempts to create toxicities models have been made, simply measuring the 3D dose distribution on organ at risks by equivalent uniform dose (EUD) or mean dose. Advances in computing and the availability of many Machine Learning algorithms allow to catch complex interactions between dose and non-dose factors. Aim of this study was to test an 'in house software' to elaborate predictive model on prostate cancer patients treated in exclusive setting.

Materials and Methods: A prospective study was performed on prostate cancer patients, treated with volumetric Arc Therapy radiotherapy and Image guided radiotherapy technique. We delivered moderate hypofractionation with a simultaneous integrated boost (SIB). Clinical Target Volume (CTV) included: prostate (CTV1, 80 Gy) and seminal vesicles (CTV2, 72 Gy) in the largest part of sample. Cumulative dose-volume histograms (DVHs) of calculated treatment plans were exported from the Eclipse TPS. Data were analyzed by a software package, written in R and internally developed, called MODDICOM. By specific functions created *ad hoc*, we analysed the impact of Vdose for gastrointestinal and genitourinary toxicity, both acute and late (using RTOG and CTCAE 4.0 scales). Dose from treatment planning and simulated delivery was evaluated to calculate the Niemierko's EUD-based NTCP and TCP values. To calculate the EUD-based NTCP, we used parameterizations of the dose-response characteristics using Lyman NTCP formula.

Results:



A total of 123 patients were recruited. Using MODDICOM we found a significant correlation (Mann-Whitney Test p=0,054, Logistic Model p=0.00692, Cox Model p=0.0198) between a Vdose of 59,5 Gy and late rectal toxicity probability of Grade 1, in terms of proctitis and rectal haemorrhage from CTCAE 4.0. This result agrees with the literature, in particular with QUANTEC revision of constraints for Radiotherapy. Moreover, toxicity and rectal EUD significantly correlate (p=0.06827). A EUD based DVH-reduction method, was used by MODDICOM to compute NTCP. Our patients were distributed on or close to an S slope showing that 50% probability of late G1 rectal toxicity is present with a mean delivered uniform dose of 66,5 Gy.

Conclusions: MODDICOM, tested on this setting of patients, showed good proof of reliable, providing results according with the common criteria used to validate Radiation Treatment plans. The development of this software could help clinicians to elaborate predictive models, in order to analyze patients series for radiobiological modeling purposes.

PO-0745

Switch to PARP1-dependent endjoining: Olaparib-mediated radiosensitization in prostate cancer cells

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Purpose/Objective: Prostate cancer (PrCa) is the most common cancer for men with a ten-years overall survival (OS) between 60 and 70%. Radiotherapy, which is one of the main treatment for PrCa, is limited by normal tissue toxicity. Therefore, a further increase in OS requires a specific radiosensitisation of PrCa without further damage to normal tissue. It was tested by us whether targeting of repair of DNA double-strand breaks can be implemented for a specific radiosensitisation.

Materials and Methods: Previously, we reported a functional hierarchy between DSB repair pathways to ensure faithful and fast repair. Deregulation of this hierarchy switches the repair to an inaccurate repair mode which is PARP1-dependent (PARP1-EJ). In the current study, we investigated the hypothesis that this switch is responsible for PARPi-mediated radiosensitization in tumor cells. To that end, we firstly analyzed the radiosensitization effect of Olaparib on 15 different tumor cell lines. We characterized cells which are radiosensitized (responders) and others which are not.

Results: By analysing several different tumor cell lines it is shown by us that PrCa cell lines often shift to this DSB repair mode. As a consequence in this PrCa cell lines DSB repair is depressed when PARP1 is knocked down by the specific inhibitor olaparib (responders). In contrast, no reduction in DSB repair was seen in cells still using the classical NHEJ (non-responders). In responders inhibition of PARP1 by olaparib also results in a drastic radiosensitisation, which was not seen for non-responding tumor cells and likewise not for normal cells. It was also shown by us that this shift to PARP1-EJ results from defect in Ku-binding, which is the initial step of NHEJ. Biomarkers are now tested which can be used to detect PrCa shifted to PARP-EJ in order to identify patients which might be treated by RT in combination with PARP1 inhibition.

Conclusions: Overall our data indicate that in PrCa where DSB is shifted to the PARP1 dependent EJ a specific radiosensitisation is achieved by the PARP1 inhibitor olaparib without further increase in normal tissue toxicity.

Poster: Clinical track: Gynaecological tumours

PO-0746

Clinical outcome of carbon ion radiotherapy for FIGO stage IVA uterine cervical cancer

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