course of their RT. Here we report the acute toxicity outcomes for the phase 1b cohort of patients in this trial.
Materials and Methods: Six patients with high risk prostate cancer (PSA>20 or T3a/T3b or Gleason score ≥ 8) were recruited from Jan 2012 to April 2012. Prior to the start of RT they had all received a minimum of three months of LHRH analogue based androgen deprivation treatment. RT was delivered using intensity modulated techniques to the whole prostate (74Gy in 37fractions) and pelvic lymph nodes (60Gy in 37fractions). Patients took nicotinamide tablets (60mg/kg) one hour before RT was given, and breathed carbogen gas (98% oxygen; 2% carbon dioxide) via a tight fitting mask 10 minutes before and during the delivery of RT. Gastrointestinal and urinary toxicities were prospectively recorded before RT, at 3, and 6 months from the end of RT, and will continue to be monitored on a 6 monthly basis until patients have been followed up for a total of five years. Toxicities were graded using CTCAE version 4.0.
Results: All 6 patients completed their treatments according to protocol. The mean time between the start of neoadjuvant hormone treatment and RT was 121 days. They have all been followed up for a minimum of 3 months from the end of their RT. No grade 3 gastro-intestinal or urinary toxicity has been observed so far. Toxicity (table 1) in this population group is comparable with those seen during standard radiotherapy.
Conclusions: The addition of carbogen and nicotinamide to standard radiotherapy to the prostate and whole pelvis is well tolerated by all patients. No practical difficulty related to the administration of carbogen during RT was encountered. Recruitment into the phase II part of this trial continues.

Table 1 - prevalence of acute urinary or gastrointestinal toxicity at 3 & 6 months after RT

CTCAE Grade	1	2	3
Urinary toxicity	4 (66%)	2 (33%)	0 (0%)
Gastrointestinal toxicity	3 (50%)	1 (17%)	0 (0%)

Reference
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PO-0704
Hypofractionated transperineal proton-boost combined with external beam radiotherapy for prostate cancer
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Purpose/Objective: To evaluate the clinical outcome of a new fractionation protocol with transperineal hypofractionated proton boost of 20 Gy in daily 5 Gy fractions combined with external beam radiotherapy (EBRT) of 50 Gy in daily 2 Gy fractions for patients with localized prostate cancer (PC). Assuming a value of a/b of 3 Gy or 1.5 Gy and a value of relative biological effectiveness (RBE) for protons of 1.1, the equivalent dose in 2 Gy fractions (EQD2) for this schedule would be 87 Gy or 94 Gy respectively.
Materials and Methods: A cohort of 278 patients treated between 2002 and 2008 with PC has been followed for a median time of 5 years. Neoadjuvant androgen deprivation therapy (N-ADT) was given to 139 patients. Only 12 patients received pelvic node EBRT. A rectal retraction rod was used for 147 patients for better target coverage and immobilization. The occurrence of GU toxicities in patients with grade 0 and with grade 1 symptoms at baseline were separately analysed as they were found as strong predictive factors for developing side effects at later times. Both cumulative incidence and actuarial prevalence of GU and GI side effects were evaluated according to RTOG guidelines. The cohort included 63 low-, 95 intermediate- and 107 high-risk PC patients with a median follow-up time of 5years.
Results: The 5 and 8 year overall survival of the whole group was 89% and 71%. The 5 and 8-year probability for prostate cancer specific mortality was 0% for the low- and intermediate groups compared to 7% and 17% for the high-risk group, respectively. The 5-year probability for PSA relapse was 0%,5% and 26% for low-, intermediate and high-risk patients, respectively. The 5-year probability for distant metastases rate was 0%, 4% and 21% for the low-, intermediate and high-risk groups, respectively. Two patients had local failure. Evaluating baseline (GU) and (GI) symptoms as well as sexual functionbefore treatment was found to be important in the evaluation of side effects. Mild pre-treatment GU-symptoms were found to be a strong predictive factor for late GU-toxicity. For baseline symptom-free patients the prevalence at 3 years was 13%, 4%, and 1% for grade ≥ 2, grade ≥ 3,and grade 4, respectively. Prevalence analysis showed a decline in symptoms. At 5 years this group had a prevalence of 1%, 1%, and 1% for grade ≥ 2,grade ≥ 3, and grade 4, respectively. No patients developed grade 3 or 4 GI toxicities.
Conclusions: Hypofractionated proton boost combined with EBRT is associated with an excellent clinical outcome and low rates of treatment toxicities. Bladder toxicities rather than rectal toxicities seem to be dose limiting and determined by epithelial damage over afollow-up time of 5 years. Long-term follow-up is necessary to evaluate the evolvement of any true late progressive and irreversible injury. Perineal proton boost preferably with spot scanning may offer substantial dose escalation and allow hypofractionation be applied safely.

PO-0705
IGRT tracking prostate fiducials increases risk of acute diarrhea during whole pelvis IMRT/VMAT for prostate cancer
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Purpose/Objective: To assess the impact of IGRT modality on the risk of GR2+ diarrhea during whole pelvis intensity modulated radiotherapy for prostate cancer.
Materials and Methods: 157 consecutive pts were treated at 2 Institutions (112 pts at Institution A and 45pts at Institution B) in two non-overlapping eras under supervision of the same radiation oncologist. All pts received prophylactic whole pelvis treatment to 54 Gy in 30 fxs with either IMRT (Institution A) or VMAT (Institution B). Moreover, depending on Institutional policies and availability, daily imaging was performed on selected pts with 2 different modalities: tracking of 3 seeds in the prostate (translations only) ('fiducials') and CBCT±Exactrac aligned to bone (translations ± rotations) first and eventually to the prostate (translations only) ('CBCT'). In the latter subgroup, prostate alignment was based on soft tissues due to the lack of fiducials. Diarrhea was prospectively scored during treatment at each weekly visit and endpoint is here considered the development of GR2+ peak toxicity at any point during treatment according to CTCAE v2.0. Based on previous work (Sanguineti et al, Strahlenther Onkol, 2009), selected covariates (G2+ proctitis, yes vs no, and the absolute volume of intestinal cavity receiving at least 15Gy, IC-V15, continuum) along with daily imaging technique (no IGRT vs IGRT/fiducialsvs IGRT/CBCT) were investigated at logistic regression for their possible association with the development of peak GR2+ diarrhea. Moreover, within the IGRT/fiducials subgroup, for each pt both the systematic (average) and random (SD) errors (mm) along the 3 axes were computed and extracted.
Results: Overall 50 pts (31.8%) developed endpoint. The risk of GR2+ diarrhea was 23.5%, 25.0% and 51.1% in pts undergoing no daily IGRT, IGRT/CBCT and IGRT/fiducials, respectively (p=0.005). Compared to pts treated without daily IGRT (N=68), pts treated with daily IGRT/fiducials (N=45) had a OR of 3.4 (95%CI 1.5-7.6, p=0.003) while IGRT/CBCT was not associated with an increased risk of GR2+ diarrhea (OR=1.1, 95%CI 0.5-2.7, p=0.806). Among pts treated without IGRT or with IGRT/CBCT (N=112), G2 proctitis (OR:1.8,95%CI: 1.0-3.0, p=0.033) and IC-V15 (OR:1.1, 95%CI: 1.0-1.3, p=0.033) confirmedto be predictors of intestinal toxicity. Among pts treated with IGRT/fiducials, neither G2 proctitis or IC-V15 predicted endpoint. Interestingly, the risk of GR2+ diarrhea was significantly correlated with the individual systematic error along craniocaudal (CC) axis (OR: 1.3, 95% CI 1.0-1.6,p=0.033) and to a lesser extent along anteroposterior (AP) axis (OR: 1.2, 95%CI 0.9-1.4, p=0.066). No correlation was found with random errors.
Conclusions: In presence of systematic errors along the CC and/or AP axes, tracking the prostate only during WPRT vanishes the role of both clinical (proctitis) and dosimetric (V15) factors in predicting the risk of diarrhea during treatment.