with IMRT were considered (incidence 7%). Late G2 and G3 GU TOX were 6% vs 7% and 3% vs 3%, respectively.
Conclusions: This study provides support for the use of WPRT in combination with HDSRT in the salvage setting in node-negative patients. Especially if delivered with modern IMRT techniques, WPRT did not result in any additional toxicity.

PD-0460
Hypofractionated prostate radiotherapy: Can biological equivalent dose volumes predict late rectal toxicity?
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Purpose/Objective: Numerous authors have attempted to establish models to minimise rectal late effects following prostate radiotherapy, most using data from standard fractionation regimes with disagreement as to predictive dosimetric values. This study looked to identify predictive Biochemical Equivalent Dose (BED) volumes, applicable for any treatment regime, using various dose mapping techniques.
Materials and Methods: We retrospectively analysed dose volume data for 172 prostate adenocarcinoma patients, median age 65.1 (range 48.1-75.5), treated at a single centre between 2006 and 2009 with radical radiotherapy. All patients received 3D_CRT or IMRT according to evolving practise with dose fractions as shown in the table.

Fractionation	52.5Gy/20#	50Gy/16#	74Gy/37#	60Gy/20#	57Gy/19#
Planning	3D-CRT	3D-CRT	IMRT	IMRT	IMRT
Number	11	64	9	7	81

Rectal dose-volume histograms (DVH) and dose-surface histograms (DVS) were calculated for each patient using standard rectal contouring (ano-rectal to recto-sigmoid junction) all performed or reviewed by the author. In addition distribution of dose to the latitude of the rectum was examined by converting the rectal surface dose into a 2D structure. Dose was converted into a BED using an alpha/beta ratio of 3 for the rectum.
Each patient completed a LENT-SOMA questionnaire to assess late rectal toxicity. For this study answers regarding issue with constipation or diarrhoea were not considered as this was not felt to represent true late rectal toxicity alone. Partition analysis was performed for all data and for IMRT alone to establish if there was a BED and volume for any given mapping technique that was statistically significant in predicting late rectal toxicity (score ≥2).
Results: Partition analysis from 0-100% of volume was performed at BED levels of 120Gy, 110Gy, 100Gy, 90Gy, 80Gy, 70Gy and 60Gy. At all of these doses there was no percentage volume of rectum receiving a given dose that was predictive for the development of late rectal toxicity regardless of dose mapping method and radiotherapy technique used.
Conclusions: This study does not support the hypothesis that incidence of toxicity significantly increases above threshold dose/volumes using BED. This conflicts with previous studies looking at dose volume in standard 2Gy per fraction and others looking at the use of Equivalent Uniform Dose to normalise data from varying fractionation regimes. The use of lateral dose distribution has not been shown to have any additional predictive power over conventional dose mapping. This may in part be due to unaccounted for movement of the rectum during treatment comprising dose mapping data. Further ongoing study is attempting to quantify this degree of intra-treatment movement and will be reported when available.

PD-0461
Characterization of nodal metastases in prostate cancer patients at high risk for lymph node involvement
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Purpose/Objective: The aim of the present study was to investigate the diagnostic gain in the detection of lymph node (LN) metastases by means of immunohistochemical (IHC) staining for pankeratin as compared to the routine histopathological evaluation. In addition, E-Cadherin (ECad) expression was investigated within the concept of epithelial mesenchymal plasticity.
Materials and Methods: Forty patients with a risk ≥10% but <35% for LN metastases (Partin tables) who were N0 at contrast-enhanced CT-scan and did not receive any prior treatment were included in the study. They all underwent a superextended LND followed by radical prostatectomy (RP). All LN (n=838) were completely serially sectioned at 300µm and stained for pankeratin (n=4498), in addition to one central H&E-stained section per LN. Disease positivity was defined as the presence of any metastatic deposits in a LN and classified as follows: Macro+ (> 2mm), micro+ (<2 mm but >0.2 mm) and ITC (< 0.2mm). ECad staining was performed on the diagnostic biopsies (n=36), RP specimens (n=39) and on the pankeratin-positive LN sections. Staining intensity was scored as negative/weak (1), moderate (2) or strong (3) and the staining pattern as inhomgeneous (0) or homogeneous (1). In case of staining heterogeneity, the most prevalent staining intensity was scored (Table 1).
Results: Sixteen out of 40 (40%) patients were found to be node-positive (N1) after routine H&E analysis. More specifically, 44 (5.3%) affected LN were found in which 25 Macro+, 19 micro+ and 9 ITC were detected. Step-section IHC analysis with pankeratin revealed metastatic disease in 2 patients that were previously N0. In each of these patients 1 affected LN was found, i.e. 1 LN harbouring a micro+ as well as a group of ITC and the other one harbouring only 1 group of ITC. Four additional affected LN in which micro+ and/or ITC were detected, were found in 3 patients that were already N1. Altogether, this detailed IHC analysis resulted in 50 (6.0%) affected LN, i.e. 25 Macro+, 24 micro+ and 17 groups of ITC, that were found in 18/40 (45%) patients. The majority of biopsies (92%) and RP specimens (79%) showed strong, homogeneous ECad expression. In contrast, ECad expression in the LN was found to be weak in about 60% of all cases. While the ECad staining pattern in the ITC and micro+ was mainly homogenous, the Macro+ showed a much more heterogeneous pattern (Pearson Chi-square p <0.0001).

Table 1. E-Cadherin expression in biopsies, RP specimens and LN metastases

	Biopsy			RP specimen				Biopsy		RP specimen	
Staining	1	2	3	1	2	3	Pattern	0	1	0	1
pN0	0	1	19	1	2	18	pN0	6	14	6	15
pN1	0	2	14	2	3	13	pN1	5	11	4	14

	LN metastases				LN metastases	
Staining	1	2	3	Pattern	0	1
ITC	11	6	0	ITC	0	17
Micro+	13	7	4	Micro+	9	15
Macro+	16	6	3	Macro+	21*	4

* p < 0.0001 Pearson Chi-square

Conclusions: IHC analysis of serially sectioned LN increased the detection rate of pelvic LN metastases only marginally. This labour-intensive and expensive procedure cannot be recommended as long as the clinical relevance of micrometastatic disease and ITC is not proven. Indicative to this could be the difference in ECad staining homogeneity between the ITC/micro+ and Macro+. The different staining intensities in the Macro+ may indicate an ongoing mesenchymal epithelial transition, presumed to be a mechanism for metastatic colonisation [Wells A 2008].

PD-0462
Post-prostatectomy WPRT does not increase the risk of second cancers: A single institution analysis of 953 patients.
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Purpose/Objective: Whole-pelvis radiotherapy (WPRT) may have a role both in the adjuvant (ADV) and salvage (SALV) setting after radical prostatectomy (RP) for prostate cancer (PCa). Aim of this analysis was to investigate a possible role of WPRT in increasing the risk of radiation-induced second neoplasms (2ndNPL) in the post-prostatectomy setting.

Materials and Methods: From 1993 to 2007, 953 patients (median age 65 years) underwent ADV (n=685) or SALV (n=268) RT with non conformal (n=169), 3DCRT (n=658) or IMRT (n=20) technique at 1.80 Gy/fraction, at a median RT dose of 70.2 Gy, or moderately hypofractionated (median 28 fractions) Tomotherapy (n=106) to a median 2-Gy equivalent (EQD2, a/b=3) dose of 70 Gy. WPRT was delivered to 282 patients at a median of 50 Gy. The median follow-up (FU) of pts treated with prostatic bed (PB) only RT was longer (110 *vs* 85 months) as compared to the WPRT+PB group.
Results: After a median FU of 103 months, actuarial 10-year overall survival (OS) was 86%. A 2ndNPL arose in 101 patients after a median of 46 months from RT (44/101 after >5 years). Thirty-two were INFIELD and 69 were OUTFIELD. The 10-year overall risk of 2ndNPL was 14% *vs* 9% (p=0.10) for pts receiving PB only or WPRT+PB, respectively (4% *vs* 2%, p=0.17, for INFIELD and 9% *vs* 6%, p=0.33, for OUTFIELD). Of note, the 10-year risk of 2ndNPL was significantly higher (17% *vs* 11%, p=0.02) in patients experiencing any (acute or late) GU toxicity Grade ≥2. Multivariate analysis, which indicated the independent predictive role of age >65 year in all subgroups, confirmed Grade ≥2 GU toxicity as a significant predictor of the risk of overall (HR 2.15, p=0.04) and OUTFIELD (HR 2.10, p=0.04), but not INFIELD 2ndNPL. When the analysis was limited to 2ndNPL onset after >5 year from RT, diabetes emerged as the only independent predictor of overall 2ndNPL (HR 2.19, p=0.048) and age >65 that of OUTFIELD ones (HR 1.08, p=0.02), while no factors independently predicted INFIELD 2ndNPL (n=13). Overall, 123 pts died, 53 owing to PCa progression, 34 to a 2ndNPL and 36 to non neoplastic causes. The 10-year risk of death was quite similar in pts experiencing a clinical relapse of PCa or an INFIELD or OUTFIELD 2ndNPL (40% vs 31% *vs* 37%, respectively, p=0.48) and significantly higher than that (6%) of pts bNEDs or with a PSA failure only after RT. Importantly, no role emerged for RT dose, technique or fractionation.
Conclusions: Although preliminary, this study suggests that the impact of treating larger volumes with WPRT may be not significant, in contrast with the hypothesis of a proportionally higher incidence of 2ndNPL with the increase of body integral dose. The correlation which emerged between GU toxicity and the risk of 2ndNPL deserves further investigation.

PD-0463
Radical radiotherapy in high-risk prostate cancer patients with high or ultra-high initial PSA levels.
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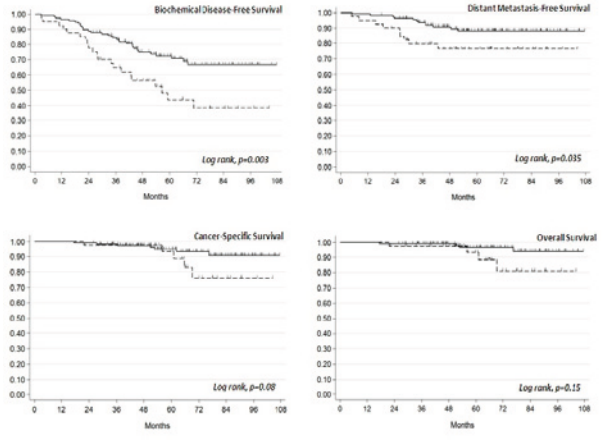
Purpose/Objective: Purpose of this study is to analyze outcomes and pre-treatment prognostic factors in high-risk prostate cancer patients with initial PSA ≥ 20 ng/mL, treated with high-dose External-Beam Radiotherapy (EBRT) and androgen-deprivation therapy (ADT) in a single institution.
Materials and Methods: Between March 2003 and December 2011, 155 consecutive high-risk prostate cancer patients a) presenting with pretreatment PSA level ≥ 20 ng/mL, b) treated with definitive EBRT and c) with a minimum follow-up of 24 months were included in this retrospective analysis. Phoenix definition was used to define biochemical control. Multivariate analysis was performed to determine the independent prognostic impact of pre-treatment clinical factors (T stage, PSA and Gleason Score [GS]) on clinical outcomes (biochemical Disease-Free Survival [bDFS], Distant Metastasis Free Survival [DMFS], Cancer-Specific Survival [CSS], Overall Survival [OS]).
Results:



	Biochemical DFS		DMFS		CSS		OS	
	Univariate	Multivariate	Univariate	Multivariate	Univariate	Multivariate	Univariate	Multivariate
PSA	0.003	0.027 (HR: 1.8)	0.03	NS	NS	NS	NS	NS
Gleason Score	0.003	0.022 (HR: 1.6)	NS	NS	0.05	0.044 (HR: 4.2)	NS	0.038 (HR: 2.6)
T stage	NS	NS	NS	NS	NS	NS	NS	NS

Table 1. Univariate and Multivariate analysis (Biochemical Disease Free Survival, bDFS; Distant Metastasis Free Survival, DMFS; Cancer Specific Survival, CSS; Overall Survival, OS)

At a median follow-up of 62 months, actuarial bDFS, DMFS, CSS and OS at 5 years were 64.8%, 85.2%, 95.8%, and 94.4%, respectively. On multivariate analysis, only GS was significantly associated with three clinical endpoints (bDFS: HR 1.6; *p=0.022*, CSS: HR 4.27, *p=0.044*, OS: HR 2.6;*p=0.038*). Pre-treatment zenith PSA (zPSA) was associated only with bDFS (HR 1.87; *p=0.027*).
Conclusions: Patients with 'high' PSAl evels (≥20 ng/mL) or 'ultra-high' PSA levels (≥ 50 ng/mL) showed favorable clinical outcomes, supporting thus the role of local radiotherapy as primary therapy in combination with long-term ADT in patients with high PSA levels at diagnosis. As GS of 8-10 resulted to be the strongest predictor of outcome, a subgroup of patients at worse prognosis might be early identified, since these patients represent the ideal candidates for more tailored and aggressive therapies in future trials.

PD-0464
Assessing response to chemotherapy with diffusion weighted MRI (DW-MRI) in muscle invasive bladder cancer (MIBC)
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Purpose/Objective: Neo-adjuvant chemotherapy (nCT) has known survival benefit in the treatment of MIBC. Favourable response is associated with improved outcome and identifies those who may benefit from bladder preservation with radical radiotherapy. Conventionally response assessment is with cystoscopy. We report on the use of DW-MRI as a potential non-invasive alternative means of assessment and as a predictor of nCT sensitivity.
Materials and Methods: 19 patients with confirmed MIBC suitable for nCT were recruited prospectively to an ethics approved protocol. DW-MRI was performed on a 1.5T system using b-values 0,50,100,250,500 and 750s/mm^2 prior to and on completion of nCT. Tumour was drawn on the 750s/mm^2 image and transferred onto the corresponding ADC map to record mean values. Following final DW-MRI patients proceeded to cystoscopy ± biopsy. Association between nCT sensitivity, pre-treatment ADC, post-treatment ADC and change of ADC (ΔADC) was analysed.
Results: 12 patients achieved pathological complete response, 6 achieved partial response and 1 progressed following nCT (as assessed on cystoscopy and T2-weighted MRI). In 15 patients tumour was identified on pre-nCT DW-image. 4 patients had no measurable disease on pre-nCT MRI. Baseline tumour median ADC was 1.3x10^{-3}mm^2/s (range 0.7-2.7x10^{-3}mm^2/s).
Complete response was associated with a significant increase in median ADC from 1.3x10^{-3}mm^2/s (range 0.7-2.7x10^{-3}mm^2/s) to 2.2x10^{-3}mm^2/s (range 1.9-3.2x10^{-3}mm^2/s) (p=0.036). Change in mean ΔADC was significantly greater in complete responders compared to incomplete responders; responders median ΔADC 1.1x10^{-3} mm^2/s, range 0.6-1.41x10^{-3}mm^2/s; incomplete responders median ΔADC 0.1x10^{-3}mm^2/s, range 0.03-0.3x10^{-3}mm^2/s (p=0.034).
Pre-treatment ADC was not predictive of response to nCT.