First author, Journal (year)	Population (risk factor)	Technique	N. Pts	Dose prescription	Median follow-up	Toxicity & Outcome
D'Amico, IJROBP (1998)	- T1cNxM0; - PSA < 10 ng/mL; - Biopsy Gleason score ≤ 3+4; - MRI stage T2 disease	MR-guided ^{125}I implant	9	Min. dose to peripheral zone = 160 Gy.	2 months	Minimal acute morbidity.
Albert, Cancer (2003)	MRI-guided BRT: - T1c; - PSA < 10 ng/mL; - Biopsy Gleason score ≤ 3+4; - MRI T2 disease; MRI-guided BRT + EBRT: either PSA > 10–13 or ≥ 50% positive biopsies or MRI evidence of extracapsularity.	MRI-guided BRT or MRI-guided BRT + EBRT	201	MRI-guided BRT: min. dose to peripheral zone = 160 Gy. MRI-guided BRT + EBRT: min. dose to peripheral zone = 77 Gy; 45 Gy with 3D-CRT	2.8 years	Mono-therapy vs. combined modality therapy: Rectal bleeding: G1 80% vs. 85% (Pvalue ns), G2 18% vs. 22% (Pvalue ns), G3 8% vs. 30% (Pvalue = 0.0001). Erectile dysfunction: 82–93%. Bladder/urethral dysfunction: no late events after monoth. Cystitis in 2 patients after combined-modality therapy.
D'Amico, Urology (2003)	- T1c; - PSA < 10 ng/mL; - Biopsy Gleason score ≤ 3+4; - No perineural invasion on biopsy.	Prostatectomy vs. MR-guided BRT	322 vs. 196	< 100% of the PD to anterior base and zone anterior to urethra; > 100% of the PD to peripheral zone	4.2 years vs. 3.95 years	5-year estimate of PSA control: 93% vs. 95% (ns) after RP or brachytherapy, respectively.
Vainshtein, Radiation Oncology (2012)	- Gleason score ≤ 6; - PSA ≤ 10; - T1c-T2a; - Excluded if on androgen deprivation therapy	Standard EBRT (S-IMRT) vs. urethral sparing IMRT (US-IMRT)	16	75.85 Gy in 41 fractions	56 months	No differences in EPIC urinary domain HRQOL summary or subset scores. No differences in the bowel, sexual, hormonal, or satisfaction domain scores. Mean PSA nadir 1.5 vs. 0.78 ng/ml (p=0.05) in US-IMRT vs. S-IMRT. 2-year PSA failure rate: 25% in US-IMRT, 0% in S-IMRT.
Barret, European Urology (2013)	- T2a or less - PSA < 10 ng/ml; - Gleason sum ≤ 6; - Unilateral disease; - Fewer than 3 positive biopsies.	^{125}I-BRT (12 pts), HIFU (21 pts), VTP (23 pts), cryotherapy (50 pts)	106	145 Gy	9 months	13% treatment-related complications: 2 G3b. Median IIEF-5 = 14, median IPSS = 6.
Cosset, Brachytherapy (2013)	- life expectancy superior to 10 years - T1c or T2a - PSA < 10 ng/mL - Gleason score ≤ 7 (3+4) - Unilateral disease - No individual biopsy core with more than 50% involvement. Total of prostate volume < 60 cc - IPSS ≥15	^{125}I-BRT	21	145 Gy	28 months	Mean IPSS: 5.4, 11.8, 6.6, 6.1 @ baseline, 2-6-12 mo. No rectal toxicity at 6 and 12 mo. Mean IIEF: 20.1, 18.6, 19.1, 19.8 @ baseline, 2-6-12 mo. Mean PSA: 6.9, 5.5, 3.2, 2.6 ng/mL @ baseline, 2-6-12 mo. Negative biopsies in 5 pts, a Gleason 6 (3+3) lesion <1mm in one patient contra-laterally.
Nguyen, The Journal of Urology (2015)	- T1c - PSA < 15 ng/ml - Biopsy Gleason score ≤ 3 + 4	Monotherapy with MRI-guided ^{125}I-BRT or MRI-guided ^{125}I-BRT + EBRT (61 pts)	318	Monotherapy: prescribed dose = 137 Gy. MRI-guided ^{125}I-BRT + EBRT: 45 Gy in 1.8 Gy/fr to prostate and seminal vesicles, followed by a BRT boost to 90 Gy.	61 months	Using nadir +2 with PSA >0.75ng/ml per year, PSA failure-free survival 91.9% at 5 years and 86.2% at 8 years. For intermediate risk cases: failure-free survival 73.0% at 5 years and 66.4% at 8 years. Distant metastases developed in 1 patient.

Conclusion: Despite the numerous publications on focal therapy in prostate cancer, primary FRT is largely unexplored. Radiotherapy appears to be particularly suitable as a focal approach, since it has an established biological basis, known tumoricidal activity, possibility of dose differentiation, large availability of high-precision dose delivery techniques, limited or no invasiveness and familiarity to radiation oncologists and urologists. However, when applied as primary FRT, its use remains investigational since numerous questions remain unmet: consensus on the initial diagnostic tools, the optimization of technical parameters for therapy delivery, follow-up exams and scheduling, tumour control and toxicity profile, response evaluation and failure definition, salvage therapy and cost-benefit.

EP-1381

ADC of prostate tumour and normal tissue during radiotherapy after neoadjuvant hormone therapy

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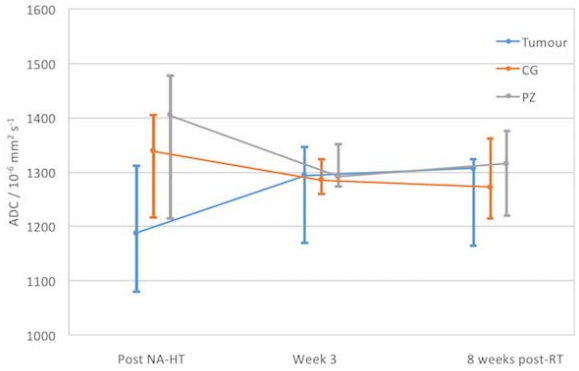
Purpose or Objective: Changes in prostate and tumour ADC values during radiotherapy (RT) may aid prediction of response to treatment. Intermediate and high risk patients are likely to receive neoadjuvant hormone therapy (NA-HT) prior to RT, causing reduction in prostate and tumour volume and changes in ADC values. It is unclear how this affects further ADC changes during subsequent treatment. We assessed ADC values in prostate tumour and normal tissue during RT after NA-HT.

Material and Methods: Fifteen patients with≥T2b disease who were due to receive RT (60 Gy in 20 fractions) were recruited after 3 months of NA-HT. Patients underwent three 1.5 T MRI examinations: post NA-HT (one week prior to RT), at the end of the third week of treatment, and eight weeks after RT completion. The imaging protocol included T2 weighted and diffusion weighted imaging, acquired using the cardiac coil (EPI with TR/TE 8000/70 ms, b = 100, 400, 800 s/mm²). ADC maps were processed offline (ADCmap for Osirix). Normal central gland (CG), peripheral zone (PZ) and tumour were outlined on T2w images by a radiologist expert in prostate MRI, with pre-NA-HT imaging (T2w and DWI) available in 12 patients to aid identification. If disease was not clearly visible, clinical findings and biopsy results were used to aid delineation. CG, PZ and tumour regions were transferred to the ADC maps and median values extracted along with interquartile ranges. A Mann-Whitney U test was used to analyse differences between tumour and normal tissue regions at the three time points.

Results: 13 patients completed all scans, 2 patients missed 1 and 2 scans respectively. After NA-HT, there was a significant difference between median tumour and PZ (p=0.009) and tumour and CG (p=0.002) (median values plotted in figure 1). At the other time points, there was no difference between tumour and normal tissue ADCs.



Conclusion: The ADC values display a similar pattern to that seen in previous studies for patients receiving RT alone. The difference between tumour and normal tissue was smaller at baseline than has been seen in other work without NA-HT. This may be due to a reduction in normal tissue ADC during induction therapy, whilst tumour ADC values could have increased due to tumour shrinkage. Variation in imaging protocol for ADC measurement compared to previous studies may also play a role. The reduced magnitude of changes in tumour ADC seen during RT after NA-HT may make its use as a predictive tool for treatment response more challenging in this group of patients.

EP-1382

PET/CT and MRI guided salvage radiotherapy after prostatectomy for prostate cancer

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Purpose or Objective: At the time of a biochemical recurrence after prostatectomy it is important to distinguish patients who have a local recurrence from patients with distant metastasis. PET/CT and MRI are important imaging modalities that can be used in this scenario. The purpose of this study was to investigate the outcomes and toxicities of patients in a large single-institution cohort treated with salvage radiotherapy (sRT) and dose escalation up to 72 Gy. Boost planning was based on MRI or PET/CT.

Material and Methods: From 2008 to 2012 290 patients who received sRT were included into the analysis. Patients with a PSA > 1 ng/ml or a PSA doubling time > 3 months received a Choline PET/CT before the start of radiotherapy. Additionally, in most patients MRI of the pelvis was conducted. If there was a macroscopic tumor recurrence, defined as local recurrence in the prostate bed in MRI or PET tracer uptake, radiation therapy to the prostatic bed was

complemented by a boost to local recurrence to a total dose of 72 Gy. In case of no macroscopic tumor recurrence the total dose was 66.6 Gy.

Results: MRI was performed in 233 patients and PET/CT was performed in 169 patients. A local recurrence in the prostate bed could be detected in 123 patients with a median volume of 0.5 ml (range, 0.03 – 125.00 ml). The median follow-up time after RT was 49.4 months (range, 7.3 – 86.1 months). A total of 85 patients experienced a biochemical failure with a median time of 19.8 months (range, 1.9 – 76.1 months) after sRT. Median PSA level at the time of recurrence was 0.91 ng/ml (range, 0.01 – 2224.00 ng/ml). The median BRFS after radiation therapy was 73 months. The estimated 3- and 5-year bRFS was 72% and 55%, respectively. On multivariate analysis, Gleason Score (hazard ratio, 6.946; p = 0.006) and pre-RT PSA level (hazard ratio, 2.265; p = 0.022) were statistically significant predictors for bRFS. bRFS was similar in patients with a macroscopic recurrence in either MRI or PET/CT compared to patients without a macroscopic recurrence. 5-year overall survival was 91% and 5-year cancer-specific survival was 96%. Grade 3 gastrointestinal toxicity was observed in 4 patients and 3 patients showed grade 3 genitourinary toxicities. No grade 4 gastrointestinal or genitourinary side effects were reported.

Conclusion: Gleason score and pre-RT PSA were important predictors for bRFS. The dose in salvage radiotherapy should be increased to 72 Gy to prevent an early recurrence after sRT in patients with a macroscopic recurrence. A higher total dose of up to 72 Gy was well tolerated in this cohort of patients.

EP-1383

PSA kinetics in prostate cancer patients after SBRT radiotherapy using CyberKnife.

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Purpose or Objective: The aim of the study was to assess the kinetics of the Prostate-Specific Antigen (PSA) in prostate cancer patients after stereotactic body radiotherapy using CyberKnife System.

Material and Methods: 44 localized prostate adenocarcinoma patients (33 low and 11 intermediate risk) without hormonal therapy, were irradiated using the CyberKnife Radiosurgical System. The prescription dose was 36,25 Gy in five fractions. During the 1-year follow-up all the patients had at least six PSA measurements – before the treatment (1-2 months before RT), during RT (after the 4th fraction) and 1, 3, 6, 12 months after RT.

Results: The mean initial PSA value among the patients was 6,25 ng/ml (range from 3,02 to 17,46 ng/ml). During the treatment we observe the PSA increase – the mean value was 11,89 ng/ml (4,13-30,68ng/ml, 155% of the initial PSA in average). In every case we noticed the PSA nadir 12 months after the treatment with a mean value of 1,50 ng/ml (0,10-4,56 ng/ml). The mean slope of the PSA was 0,56 ng/ml/month (median 0,46 ng/ml/month). No biochemical failure was observed.

Conclusion: The PSA kinetics after treatment can reflect the biological effect of radiation on prostate cancer and potentially correlate with a clinical outcome. Especially the lower value of PSA nadir (<0,5 ng/ml) is considered to associate with an increased freedom from biochemical failure. The interpretation of PSA slope is more controversial however some studies indicates a correlation with clinical outcome. Our results are similar to other SBRT studies and significantly better than in conventionally-fractionated technics. The rapid decline in PSA is particularly worth to be underlined. The further follow-up will probably confirm the expected good clinical outcome.

EP-1384

Acute toxicity hypofractionated-IMRT vs standard radiotherapy in prostate cáncer: comparative study

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Purpose or Objective: To describe and compare acute toxicity rate in three different radiotherapy (RT) protocols for prostate cancer (PC): hypofractionated radiotherapy intensity modulated and image-guided radiation therapy (Hypo-IMRT-IGRT) group A: 21 fractions/3Gy and group B: 28 fractions/2.5Gy) and three-dimensional conformal radiotherapy standard fractionation (3DCRT) group C: 39 fractions/2Gy.

Material and Methods: Patients with the diagnosis of PC treated with RT between January 1st 2011 to June 30th 2015 were included. Hypo-IMRT-IGRT were performed using internal marker and ExacTrac-X-Ray-system. In 3DCRT group not employed internal marker. Acute genitourinary (AGUT) and acute gastrointestinal toxicity (AGIT) were assessed according to RTOG-EORTC criteria. A p value<0.05 was considered significant. Results were expressed as median (IQR). Categorical and continuous variables were compared with X2 and kruskal-Wallis ran sum test respectively. All statistical analysis was performed using R package. The institutional review board approved this study.

Results: 242 consecutive patients were retrospectively analyzed (group A: 39, group B: 128 and group C: 74). No baseline characteristic differences were found (age, PSA, TNM, PTV total, bladder and rectal volume). Maximal bladder doses and V60 rectal were different within the three groups (p=<0.01). AGUT (n): in group A was grade 0: 18; grade 1: 9, grade 2: 12; group B grade 0: 35; grade 1: 86; grade 2: 7; and group C grade 0: 23; grade 1: 38; grade 2: 13 (p=<0.01). AGIT was in group A grade 0: 38; grade 1: 1; grade 2: 0; group B grade 0: 121; grade 1: 7; grade 2: 0; and group C grade 0: 65; grade 1: 6; grade 2: 3 (p=0.07) Table 1. Comparative AGUT between A+B vs. C did not differ. AGIT in A+B group was less frequent than C group (p=0.017). AGUT from group A was different from group B (p=<0.01). AGIT from A group was not different from B group (p=0.75).There were no events > grade 3 reported in any group.

GRADE n(%)	0	1	2	p
AGUT				<0.01
Group A	18(46)	9(23)	12(31)	
Group B	35(27)	86(67)	7(5)	
Group C	23(31)	38(51)	38(51)	
AGIT				0.07
Group A	38(97)	1(3)	0(0)	
Group B	121(95)	7(5)	0(0)	
Group C	65(88)	6(8)	3(4)	

Conclusion: Hypo-IMRT-IGRT was associated to lower AGIT rate than 3DCRT. Hypo-IMRT-IGRT 21 fractions/3Gy was inferior to Hypo-IMRT-IGRT 28 fractions in terms of AGUT.

EP-1385

A comparative study between radical RT and radical prostatectomy in locally advanced prostate cancer

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