and EF-CCRT (42 patients) followed by high dose rate brachytherapy. Data regarding the safety profile, response rates and occurrence of local, para-aortic or distant failure were recorded.
Results: Witha median follow-up time of 5 years (range, 4-5.5), EF-CCRT (38 patients) was associated with better 5-year disease-free survival of 80.3% compared with 69.1% in 36 patients treated with WP-CCRT (p = 0.04). The PALN control rates were 97.1% and 82.1% in EF-CCRT and WP-CCRT respectively (p = 0.03) and distant control rates were 94.7% in EF-CCRT and 80.6% in WP-CCRT (p = 0.02). The 5-year overall survival rates were 72.4% for EF-CCRT and 60.4% for WP-CCRT (p = 0.04). No difference in acute toxicity profile was seen in both groups and during a median follow up of 60 months, one patient (2.6%) in EF-CCRT group experienced intestinal obstruction.
Conclusions: Prophylactic EF-CCRT showed better para-aortic nodal, distant control, disease-free survival, and overall survival rates as those of WP-CCRT with acceptable toxicity in patients with radiologic negative PALN locally advanced cervical cancer.

PD-0607
Diffusion Weighted MRI for prediction of local failure in locally advanced cervical cancer
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Purpose/Objective: Diffusion Weighted MRI (DW-MRI) is used for diagnostic cancer imaging and may have value for monitoring of tumor response to radiotherapy (RT). In this study, DW-MRI was evaluated as a non-invasive biomarker for prediction of local failure in RT of locally advanced cervical cancer.
Materials and Methods: 52 patients were treated with 45-50Gy whole pelvis external beam RT (EBRT) and 2 fractions of brachytherapy (BT). Patients underwent MRI examination 3 times during treatment with the BT applicator in situ: 1) a preplanning MRI (BT0) one week prior to first BT, 2) at time of first BT and 3) at time of second BT (BT2) one week after first BT. Dose-planning for BT was based on T2-weighted MRI following the GEC-ESTRO guidelines. DW-MRI (b=0, 600, 1.000 s/mm2) was included in all three MRIs using a 1.5T MRI. Median follow-up time from start of treatment was 24 month (min/max: 6/46 month). Blinded visual assessment of signal intensities on DW-MRI, b=1.000 s/mm2 at time of BT0 was evaluated for hyper-intensity at tumor site and was found in 22/52 patients (table 1).Images of Apparent Diffusion Coefficients (ADC) were calculated for the 22patients. The relationship between local failure and ADC, change in ADC and volumes was investigated.
Results: There was asignificant correlation between local failure (Fischer's exact test p=0.021) and presence of hyper-intense signal on DW-MR images at b=1.000 s/mm2 at time of BT0 (Table 1). The ADC for DWI ROI at BT0 in patients with local control (1.21±0.19 x10-3 mm2/s) compared to failures (1.31±0.24 x10-3 mm2/s) was not significant(p=0.21). There was no significant change in ADC from BT0 to BT2 (p = 0.44).There was a significant decrease in the volume of the DWI ROI for both patients with local control (VBT0 = 5.06±4.72 cm3 to VBT2= 1.51±1.36 cm3) (p = 0.016) and failures (VBT0= 7.54±5.02 cm3 to VBT2 = 4.12±3.12 cm3) (p =0.003). The mean DWI ROI volume at time of BT2 was significantly larger (p=0.006)in patients with failures as compared to those with local control.

Table 1	Local control	Local failure
Hyper-intense signal@BT0	14	8
No hyper-intense signal@BT0	21	1
Non-evaluable (bad image quality)	8	0

Conclusions: The presence of hyper-intense tumor signal at highly diffusion sensitive images (b = 1.000s/mm2) at time of BT seems to be a strong indicator for increased risk of persistent local disease or local recurrence. However, the qualitative and subjective nature of the visual evaluation of hyper-intense signal at DW-MR images is an issue that should be addressed in future work. At this time of treatment the ADC appears stable before and after the BT fraction and it was not possible to use the ADC to differentiate between responders and non-responders. The study shows that the tumor delineated by the DWI ROI decreases during treatment although the ADC value did not change. This study indicates that DW-MRI may be of value for monitoring RT-treatment and predicting local failure already during treatment.

PD-0608
Risk of metastasis and death in rectal cancer is increased with 8p deletion but not with gene expression
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Purpose/Objective: This study aims to determine candidate genes and chromosomal imbalances capable of predicting metastasis occurrence in a homogenous population of patients with rectal cancer.
Materials and Methods: Fresh frozen tumor tissues from 80 patients with rectal cancer were analyzed using Affymetrix HG-U133 Plus 2.0 gene expression arrays and high-resolution Illumina single nucleotide polymorphism (SNP) arrays. Median follow-up was 102 (1-146) months. Endpoints of the study were metastasis-free survival (MFS) and cancer-specific survival (CSS). The prognostic value of two validated colon gene expression signatures was also tested in this cohort.
Results: We were unable to derive a significant predictor of prognosis based on gene expression, since only a few genes were significantly associated with MFS or CSS after multiple testing corrections. In contrast, deletions of 8p and 1p36-35 correlated with worse MFS (*P = 0.005* and *P = 0.01*, respectively) and CSS (*P = 0.001* and *P = 0.01*, respectively). Multivariate analysis identified -8p as an independent prognostic factor for MFS (*P = 0.04*) and CSS (*P = 0.003*). A genomic signature of colon cancer was not significantly associated with prognosis, whereas another one significantly predicted MFS in T3 tumors (*P = 0.04*).
Conclusions: This study shows for the first time in rectal cancer an independent correlation of -8p with MFS and CSS. Specific prognostic factors may apply to rectal cancer, justifying the need for homogeneous rectal cancer samples in prognostic studies.

PD-0609
A comparison of 4 target volume definitions for pancreatic cancer: 2 with and 2 without lymphatics
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Purpose/Objective: Target volume definitions for radiotherapy in pancreatic ductal adenocarcinoma (PDAC) vary substantially. Some groups aim to treat only the primary tumour whereas others include elective lymph nodes (eLN's). ELN's close to the primary tumour are often included unintentionally within the treatment volume, depending on the respective philosophies. We aimed to measure the percentages of anatomical coverage of the eLN's comparing four different guidelines.
Materials and Methods: PTVs were contoured using planning-CT's of eleven patients with PDAC based on the Oxford, RTOG, Michigan and SCALOP guidelines. CTVs included the peripancreatic, paraaortic, paracaval, celiac trunk, superior mesenteric and portal vein lymph node areas. Volumetric comparisons of coverage of all eLN regions were conducted to illustrate the differences between the 4 contouring strategies.
Results: Significant differences in PTV sizes were observed in the following order: RTOG > Oxford > SCALOP > Michigan (620, 450, 230, 160 ccm, respectively). A large variation of eLN coverage was found for the respective subregions according to the respective guidelines. The eLN areas of highest risk, i.e. posterior peripancreatic nodes were covered best in Oxford and RTOG definitions. Much of the additional volume of the latter two compared to Michigan and SCALOP was related to paraaortic and portal venous eLNs.

Conclusions: To our knowledge, this is the first study to directly compare the percentage of anatomical coverage of eLN's by four PTVs in the same patient cohort. Potential practical consequences are discussed in detail. Knowing the specific risk of each eLN region allows to derive a moderate expansion of the primary tumour volume to include eLN regions at highest risk without significant normal tissue dose increase.

PD-0610

Preoperative IMRT-IGRT with a simultaneous integrated boost in rectal cancer: report on late toxicity and outcome.

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Purpose/Objective: Preoperative chemoradiotherapy (CRT) has been established as the standard of care for patients with cT3-4 rectal cancer. However, a benefit on overall survival (OS) could not be demonstrated with the addition of concomitant chemotherapy. We explored prospectively preoperative intensity-modulated and image-guided radiotherapy (IMRT-IGRT) with a simultaneous integrated boost (SIB) as an alternative strategy, of which first results showed a limited acute toxicity profile and promising 2-year local control (LC). Here, we report clinical outcome and late toxicity after a median follow-up of 54 months.
Materials and Methods: A total of 108 patients were treated preoperatively with IMRT-IGRT using the Tomotherapy Hi-Art II system, delivering a dose of 46 Gy in daily fractions of 2 Gy to the mesorectum and draining lymph nodes, without concomitant chemotherapy. Fifty-seven patients (53%) displayed an anticipated circumferential resection margin (CRM) of less than 2 mm based on magnetic resonance imaging and received a SIB to the tumor up to a total dose of 55.2 Gy (boost group). Late side effects were scored using the National Cancer Institute Common Terminology Criteria for Adverse Events version 3.0.
Results: Grade ≥ 2 late diarrhea was recorded in 11% of the patients. The absolute incidence of grade ≥ 3 late gastrointestinal and urinary toxicity was 9% and 4%, respectively, with a 13% rate of any grade ≥ 3 late toxicity. The actuarial 5-year LC, progression-free survival (PFS) and OS were 97%, 68%, and 68%. On multivariate analysis, R1 resection (CRM ≤ 1 mm) (p=0.03) and pN2 disease (p=0.04) were associated with significantly impaired PFS and OS. Dworak grade 3-4 regression showed improved PFS on univariate analysis (p=0.03).
Conclusions: The use of preoperative IMRT-IGRT with a SIB resulted in an acceptable late toxicity profile in T3-4 rectal cancer patients. The implementation of a SIB in a patient population at risk for local recurrence yielded a high 5-year LC rate, comparable to the rates observed after preoperative CRT.

PD-0611

TRG after chemoradiotherapy for locally advanced rectal cancer: near pCR is not a good prognostic factor

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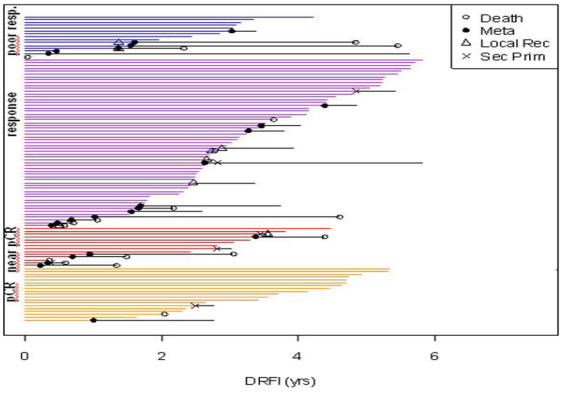
Purpose/Objective: As neoadjuvant treatment and total mesorectal excision (TME) has dramatically improved local control during the last two decades, distant recurrences now primarily determine outcome in patients with rectal cancer. The introduction of preoperative chemoradiotherapy (CRT), however, has also changed the importance of histopathological parameters. The objective of this study is to evaluate which factors determine outcome, focusing on the contribution of clinical factors and histopathological response after CRT, in the development of distant recurrences in particular.
Materials and Methods: Between 2004 and 2008, all consecutive patients with MRI-defined locally advanced rectal cancer (LARC), without synchronous metastases, treated with CRT (25x2Gy during weekdays with capecitabine 825 mg/m2 days 1-33) followed by TME after 6-8 weeks, were included. Adjuvant chemotherapy was not standard. Central revision of histopathology followed using TNM, 5th edition. Histological tumour regression grade (TRG) was scored with a 4-tier system (complete response, near complete response, response, poor response). Univariate and logrank analysis were performed to identify predictors and prognosticators.
Results: For this 107 patients with a median follow-up of 44 months, the distal recurrence free interval (DRFI), DFS and OS 3-year rates were 82%, 73% and 87%, respectively. Of the 23 patients developing distant recurrences, 11 occurred within a year after surgery (Fig 1). Slides of the resection specimens were analysed and revealed 18% pCR, 13% near pCR, 55% response, and 14% poor response. A positive CRM, ypT3-4 and presence of poor prognostic features (lymphangio invasion or perineural growth) were associated with a poor response. Four of the 19 patients with a pCR still harboured nodal metastases. Six of 14 patients with a near pCR still had ypT3 disease and 8/14 were still node positive. In addition, near pCR was associated with a relatively poor outcome: 5 out of 14 patients developed distant metastases. TRG was a powerful discriminator of DRFI, DFS and OS. In addition ypT, ypN, presence of tumour deposits (TD) and the presence of acellular mucin lakes, were associated with a decreased DRFI, and remained significant after adjusting for TRG. Whereas ypN, TD, mucinous histology and acellular mucin lakes were associated with distant recurrence within a year.



Conclusions: In this well-defined and uniformly treated cohort of LARC patients, a ypCR predicts excellent outcome, while patients with a near pCR still have a high risk of developing distant recurrences (36%). The high number of near pCR patients with ypT3 or ypN1/2 disease demonstrates that wait and see policies in locally advanced rectal cancer patients should be applied with extreme caution and care.

PD-0612

MR-guided histopathology - frequent ypT4 outcome to neoadjuvant radiation in organ-infiltrating rectal cancer

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Purpose/Objective: In rectal cancer, histopathologic complete response to neoadjuvant radiation/chemoradiation therapy (RT/CRT) commonly translates into long-term survival benefits, and some investigators are currently advocating a non-surgical 'wait-and-see' approach in patients achieving complete clinical response. Using organ-infiltrating rectal cancer as model, we aimed at identifying the actual ('true') frequency of tumor down-staging following neoadjuvant RT/CRT, by means of determining the false-negative rate of conventional histopathologic tumor response evaluation. In doing so, we developed the diagnostic procedure of magnetic resonance- (MR) guided histopathology.
Materials and Methods: Ninety-two patients that had received neoadjuvant treatment and proceeded to extended total mesorectal excision were identified from the institutional database. For each patient, the study radiologist and pathologist separately interpreted preoperative MR images and histologic preparations from the surgical specimen, to determine whether tumor down-staging had resulted. In cases of discrepancy after the separate yT staging (52 patients), histologic sections were jointly reassessed for residual tumor in areas