PD-0415
Quantitative evaluation of changes in FET PET performed during chemo-radiation of glioblastoma multiforme
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Purpose/Objective: Very limited information on how gliomas respond to chemo-radiation therapy (RCX) is available. Recent studies have shown the diagnostic potential of Positron Emission Tomography (PET) with 0-(2,18F-fluoroethyl)-l-tyrosine (FET) to discriminate glioblastoma from healthy tissue. The aim of this study was to evaluate the changes in FET uptake during RCX based on FET-PET scans.

Materials and Methods: Sixteen consecutive patients with primary glioblastoma multiforme (GBM), WHO grade IV, were treated with surgery and subsequent RCX with a standard dose of 60 Gy in 30 fractions and concurrent temozolomide (TMZ). Two FET-PET examinations, denoted FET1 and FET2, respectively, were performed once before RCX and once after approximately 20 fractions (median: 19, range 13-23). A biological tumor volume was defined in both scans (BT1 and BT2, respectively) using a threshold-based delineation, including tissue with a tumor-to-background ratio (TBR) of at least 1.6. Background was determined by contouring a large region of healthy tissue. The aim of this study was to evaluate the changes in FET uptake during RCX based on FET-PET scans. FET2 was rigidly registered to FET1 using the CT scan in order to compare uptake parameters and spatial changes of the positive volume. A maximum expansion (ME) in BT1 was calculated for each patient.

Results: After approximately 40 Gy of RCX, a significantly higher background uptake of FET was observed (p = 0.0025, paired t-test). The median change in TBRBT1 and TBRBT2 were -2.2% and -1.1% (range: -27 to +16 and -11 to +12), respectively. Investigation of the spatial change in tumor volume is illustrated in figure 1. The margin required to include BT1 at the time of FET2 ranged from 3.5 to 37 mm (median: 8.2).

Conclusions: The results show a significantly higher uptake in healthy tissue of FET during RCX, affecting the background estimate. For the 16 patients included in this study, a distinct spatial change in FET-uptake in glioblastoma during RCX was observed, assuming that the TBR of 1.6 is also usable at the time of FET2. The analysis showed a large variation of the position of the voxel with high uptake during the course of therapy.

PD-0416
Robust feature auto-segmentation of head and neck cancer
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Purpose/Objective: Definition of gross tumour volume (GTV) is of great importance for radiotherapy. Definition of GTV is performed by manual contouring on image slices from computerized tomography (CT). The GTV contours are vulnerable to intra- and inter-contourer variation. It is possible to reduce the variation by providing an automatic segmentation estimated from the image. The literature consists of approaches using differing algorithms and image features for the segmentation. In this study we investigated the implication of using different feature estimation parameters for segmentation to improve robustness of the approach.

Materials and Methods: The data set consisted of 40 patients. All patients had been diagnosed with hypopharynx cancer and were referred for radiation therapy. For each patient a PET/CT scan was available along with the contour of the GTV. These patients were divided into a training and test set consisting of 20 patients each. Image features were estimated using 4 different patch sizes, 3 ranges of values and 3 discretisation levels for both CT and PET. Tumour and background specific features were extracted from the training set. The training features were used to construct a tumour classifier using the adaboost algorithms. Repeated use of the training set using bootstrap methods ensured a robust classifier which was not influenced by outliers.

Using the classifier it was possible to extract both GTV and evaluate it against the manual contour of the test set using dice coefficient. The feature based segmentation was compared with the results of threshold segmentation on the PET image using a paired t-test, p-values of less than 0.05 were considered significant.

Results: Using the new feature approach it was possible to extract automatic GTV contours. The mean dice coefficient for the different feature settings varied from 0.65-0.80. The highest mean dice coefficient was achieved using a 3x3x3 patch with an absolute range of values ranging from -125 to 250 HU on CT and 0 to 5 SUV on PET. There was a significant difference between the feature segmentation with the lowest and highest overlap (p<0.01). Using threshold segmentation on the PET images it was possible to achieve a mean dice coefficient of 0.72. Making a paired t-test between the feature segmentation with the highest mean dice coefficient and the threshold segmentation showed a significant difference (p<0.03).

Conclusions: It was shown that it is possible to achieve a robust segmentation using image features. There is a significant difference between different feature estimation approaches. Image features produced significantly better segmentations than conventional PET-thresholding.

PROFFERED PAPERS: CLINICAL 5: GI

OC-0417
Effect of preoperative chemoradiotherapy on recurrence pattern in esophageal tumors
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Purpose/Objective: To analyze the recurrence pattern in patients with cancer of the esophagus or gastro-esophageal junction treated with either preoperative chemoradiotherapy plus surgery (CRT + S) or surgery alone (S) within the phase II and III CROSS trials.

Materials and Methods: Relapse pattern in relation to the radiation fields was analyzed in patients from the previously published non-randomized CROSS I trial (n=54) and the subsequent randomized CROSS II trial (n=368). Multivoxel treatment consisted of 5 weekly courses of Paclitaxel (50 mg/m²) and Carboplatin (AUC = 2) combined with a concurrent radiation dose of 41.1 Gy in 23 fractions of 1.8 Gy. The radiation fields included the primary tumor, all pathologic lymph nodes and an elective lymph node area of 4 cm in cranio-caudal direction from the primary tumor.

Results: Between 2001 and 2008 a total of 422 patients were included, of whom 418 were evaluable. Mean age was 60 years (36-79), histology was adenocarcinoma in 75% and squamous cell carcinoma in 23%. A total of 374 patients underwent resection (86%) of patients allocated for S and 213 (92%) for CRT+S. After a minimum follow-up of 24 months and a median follow-up of 45 months for surviving patients, the overall recurrence rate in the S-arm was 92/161 (58%) and 74/213 (35%) in the CRT-S-arm. Preoperative CRT reduced locoregional recurrences (LRR) from 34 to 14% (p<0.0001) and...
peritoneal carcinomatosis from 14% in the S-arm to 4% in the CRT+S-arm (p=0.0001). There was also a small, but significant effect on hematogenous dissemination in favor of the CRT group (35 vs. 29%, p=0.05). LRRs occurred in 5% within the radiation field, in 2% in the margins of the radiation field, and in 6% outside the radiation field while in 1% the exact site in relation to the radiation field was unclear. Only 1% of patients had an isolated infield LRR after CRT+S.

Conclusions: In patients with esophageal or junctional cancer, presurgical chemoradiotherapy improves locoregional control and reduces peritoneal carcinomatosis and has a favorable effect on hematogenous dissemination. Infield locoregional recurrences are rare.

OC-0418
SBRT for unresectable liver metastases: preliminary results of a phase II clinical trial.

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Purpose/Objective: To evaluate the feasibility of high-dose stereotactic body radiation therapy (SBRT) in the treatment of unresectable liver metastases.

Materials and Methods: Patients with one to three unresectable liver metastases with maximum individual tumour diameters less than 6cm, a Karnofsky Performance Status of at least 70, were enrolled and treated by SBRT on a phase II clinical trial. Dose prescription was 75 Gy in 3 consecutive days. SBRT was delivered using the volumetric modulated arc therapy (VMAT) by RapidArc technique. The primary end point was in-field local control. Secondary end points were toxicity, and survival.

Results: Between February 2010 and September 2011, 61 patients with 76 lesions were treated. Among them, 21 (34.3%) had stable extrahepatic disease at study entry. The most frequent primary sites were colorectal (45.9%) and breast cancer (18%). 78.7% of patients had one lesion, 18.0% and 3.3% had 2 and 3 lesions, respectively. After a median of 12 months (range 2-26 months) in-field local response rate was 94%. Median OS rate was 19 months, actuarial survival at 12 months was 83.5%. None of the patients suffered from grade 3 or higher acute toxicity. No radiation induced liver disease (RILD) was detected. One patient experienced grade 3 late toxicity at 6 months, due to ched wall pain.

Conclusions: SBRT for unresectable liver metastases can be considered as an effective, safe, and noninvasive therapeutic option with excellent rates of local control and a low treatment related toxicity.

OC-0419
Clinical complete response in rectal cancer to increase the rate of preservative chemoradiotherapy. ACCORD12 randomized trial

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Purpose/Objective: During the ACCORD12 randomized trial, a specific evaluation of the clinical tumor response of the rectal cancer following neoadjuvant chemoradiotherapy (CRT) was performed before surgery. The correlation of this end point with patient characteristics and treatment outcomes is reported.

Materials and Methods: Between 2005 and 2008 a randomized trial comparing 2 different regimens of CRT (cap45 : capecitabine + 45 Gy/5w vs capox50 : capecitabine + 50 Gy/5w + oxaliplatine) included 598 patients. A careful evaluation of the clinical response of the tumor was planned 5 weeks after the end of CRT just before surgery. Rectoscopy and digital rectal examination (DRE) was used to establish a specific score of clinical response adapted from the RECIST criteria: Clinical complete response : no visible or palpable tumor, supple rectal wall (CCR) ; partial response (PR), stable disease (ST), progressive disease (PRD). This score was correlated with patients characteristics, type of surgery, pathological response and 3-year clinical outcome.

Results: Clinical response was evaluable in 475 patients. Score was as follows : CCR : 5%, PR : 62%, ST : 29%, PRD : 4%. There was a trend toward more CCR in the capox 50 arm (6.5 % vs 3.7 %). When analysed for the whole cohort of 475 patients, CCR was associated with early T stage (T2 : 11% vs T3-4 : 5%). CCR was associated with sphincter saving surgery, ypCR, CR+, Disease Free Survival (DFS) and 3-year survival (table 1).

Conclusions: CCR appears as a very important end point after neoadjuvant treatment of rectal cancer. It is correlated with increased pCR, negative CRM, 3 year DFS and it is probably influencing the chance of a sphincter saving procedure. Rectoscopy and DRE should be performed after neoadjuvant CRT to evaluate the tumor response and adapt the surgical technique.


CCR (24 pts) % Part;Stable;Prog (451 pts) %
Sph. Sav. Surg. 21 88 % 380 71 %
ypCR 14 58 % 72 16 %
CR+ (≤1mm) 0 0 % 45 10 %
3y DFS 91 % 70 %

OC-0420
Improving quality of care in rectal cancer: the role of a central review platform in CTV delineation.

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Purpose/Objective: The increased use of high conformal radiation techniques with steep dose gradients requires a very precise definition of the clinical target volume (CTV). Although delineation guidelines are widely available, little is known about their correct implementation into daily practice. Within a national project we investigated the impact of central review on the quality of CTV delineation based on the guidelines as published by Roels et al (JROBP 2006).

Materials and Methods: Dedicated software (Aquilab, France) was installed at a central review facility and at each participating radiation oncology department. The CTV was uploaded on a secured server and centrally reviewed. In order to account for the variability in the time of inclusion between two patients in and between centres, we used a ranking system in which each 5 consecutive patients per centre were regarded as one category. This categorical patient order (cpatorder) was correlated with three volumetric parameters: kappa index (KI), volumetric ratio (RV) and commonly contoured volume (VCC). To compare the results of the volumetric parameters between the first ten patients and the others per centre a sensitive analysis was performed. A generalized linear model was used for normally distributed parameters (RV) and a regression logistic model for non-normally distributed parameters (KI, VCC).

Results: Between March 2010 and September 2012, 20 centres submitted 1255 rectal cancer cases, from which 1224 were included in the final analysis. A median of 64 patients were submitted per centre (range 6 -198). CTV was modified in 74.2% of the cases. Sensitive analysis demonstrated that there was a significant increase in RV and VCC between the first ten patients and the others (p=0.0005 resp. p=0.05) (Fig. 1). Statistical analysis did not show a sustained significant improvement in CTV delineation during the whole review period. When assessing the influence of the location of the primary tumour on CTV delineation, there was less consensus on delineation for mid seated lesions compared to low and high seated tumours. This might be explained by disagreement on which nodal volumes to include.

Part;Stable;Prog (451 pts) %
Sph. Sav. Surg. 21 88 % 380 71 %
ypCR 14 58 % 72 16 %
CR+ (≤1mm) 0 0 % 45 10 %
3y DFS 91 % 70 %