preterm stop of the therapy thus jeopardizing the intended treatment outcome. Despite numerous research attempts there is still no robust feature established in clinical routine to predict radiotherapy-induced toxicity prior to therapy start.

**Material and Methods:** The study cohort comprised 40 patients who underwent neoadjuvant radiochemotherapy (N-RCT) for rectal cancer (28x1.8 Gy, 5 times weekly, concomitant with two cycles 5-FU-based chemotherapy). From each of those patients dermal fibroblasts were cultured from skin specimen gained outside of the radiotherapy planning target volume at occasion of surgery conducted about six weeks upon N-RCT completion. Acute radiotoxicity was thoroughly monitored throughout the N-RCT series and documented according to CTC classification. Maximal acute toxicity (MAT) was defined by the highest CTC grade of the four items “cystitis”, “proctitis”, “enteritis”, and “dermatitis”. MAT was grouped into grades 0/1 (n=16), 2 (n=16), and 3/4 (n=8). N-RCT was simulated in the cultured fibroblasts for five consecutive days (1.8 Gy each at d1-d5 with addition of 5-FU at a concentration reflecting clinical steady-state levels) followed by a 7-day wash-out period. Gene expression of nine candidate genes (CAT, CDKN1A, CTGF, SMAD2/3/4/7, TGFβ1, TGFβR1) supposed to mediate early radiation-induced toxicity was ascertained by quantitative real time PCR. Samples for these RNA analyses were harvested at d2 and d5 (each 4 hours upon application of the radiation fraction) as well as at day 12 upon the wash-out period. GAPDH and HPRT1 transcript levels served as reference.

**Results:** MAT was related to radiation-induced expression changes of four of the considered genes in fibroblasts. The strongest impact was obtained for SMAD7 and CAT at d5. The higher the MAT score, the lower the induction of SMAD7 and CAT by radiation was (p=0.001 and 0.003). However, upon the wash-out period at d12 no statistical differences in dependence on the MAT score were seen anymore for these two genes. In contrast, a high MAT score was linked to low radiation-induced induction of CTGF (p=0.005) and to a faster decrease of the massively induced CDKN1A (p=0.03) at d12. At d2, a trend (p=0.06) for CAT in relation to MAT in the same direction as at d5 was noticed with no correlation of any of the other genes at this early time point.

**Conclusion:** Radiation-induced expression changes in patient-matched fibroblasts may serve as biomarkers to predict clinical radiation-induced fibrosis. The decrease of tumor hypoxia during radiotherapy. A protective role might also be attributed to sustained elevation of CDKN1A. The link between post-radiation induction of CTGF in fibroblasts and low MAT remains to be clarified. Understanding the mechanistic basis of these findings might pave the way for better protection of irradiated normal tissue.

**EP-2058**

A novel multi-SNP model predictive of erectile dysfunction following radiotherapy in prostate cancer

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**Purpose or Objective:** Erectile dysfunction (ED) is one of the most common complications encountered after radiotherapy in prostate cancer patients. The goal of this study was to investigate whether single nucleotide polymorphisms (SNPs) are associated with late ED in men treated with radiotherapy for prostate cancer. To this end, we designed a novel machine learning-based multi-SNP model using a genome-wide association study (GWAS) dataset.

**Material and Methods:** We analyzed 236 evaluable patients with at least one year of follow-up for the development of ED. The severity of ED was assessed using either the patient-administered Sexual Health Inventory for Men (SHIM) or the clinician-assigned Mount Sinai Erectile Function (MSEF) scoring schema. There were 133 patients with Grade 2 or more ED. For our analysis, the cohort was split into two groups (cases/controls: MSEF 0.1 / 2.3; cases/controls: SHIM ≥7 / ≥16). Genome-wide SNP data were available from Affymetrix Genome-Wide Human SNP Array 6.0. After a quality test including SNP missing rate<5%, minor allele frequency (MAF)<5%, and Hardy-Weinberg equilibrium (p<10E-5), 613,496 SNPs remained.

For the validation purpose of our proposed model, the dataset was split into a training dataset (2/3 of samples) and a validation dataset (1/3 of samples). Our model building process was performed using the bootstrapped data from the training dataset. Our idea is to convert the binary outcomes into preconditioned continuous outcomes based on normal tissue complication probability (NTCP) using principal component analysis (PCA) and logistic regression. The preconditioned outcomes were used in the model building process using random forest regression. Then, the model was tested using the validation dataset. The final predicted outcomes were compared with the original binary outcomes to estimate the predictive performance. We iterated this process 100 times and the performance was averaged. We compared the performance of our proposed method (preconditioning random forest regression: PRFR) with other methods including preconditioning lasso (PL), lasso logistic regression (LLR), and random forest classification (RFC).

**Results:** Univariate analysis was performed using the training dataset. With a threshold of p<0.001, 367 SNPs remained. These SNPs were fed into our model. As shown in Figure (A), the averaged performance with the validation dataset was AUC=0.62, which is better than other methods: RFC (0.57), PL (0.58), and LLR (0.57). The 79 patients in the validation dataset were binned into 6 groups according to the predicted risk of ED. Figure (B) shows the comparison of the model-predicted incidence of ED with observed incidence.

**Conclusion:** Our machine learning-based multi-SNP model showed the potential to better predict the radiation-induced late ED. However, we need to validate our model using other datasets.

**EP-2059**

Changes in hypoxia in serial F-MISO/PET-CT during chemoradiation in HNSCC

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**Purpose or Objective:** Tumor hypoxia, a common feature of locally advanced head and neck cancer (HNSCC), is associated with higher malignancy and increased radioresistance. The decrease of tumor hypoxia during
fractionated radiation treatment is assumed to be decisive for treatment success. [18F]-Fluoro-Misonidazole PET (F-MISO-PET) allows noninvasive assessment of hypoxia during treatment. The purpose of the present study was to noninvasively assess the time course of tumor hypoxia.

**Material and Methods:** A prospective serial imaging study was conducted in patients undergoing definitive chemoradiation (dRCTx, total dose 70 Gy) for locally advanced HNSCC, accompanied by cisplatin in weeks 1, 4 and 7. Tumor hypoxia was assessed by F-MISO-PET by static scans acquired 2.5 h p.i. Tumor volumes were determined for FDG PET/CT scans and the coregistered F-MISO/CT scans. At baseline MRI, FDG-PET/CT and F-MISO-PET were acquired (week 0). Additional F-MISO-PET/CT scans were acquired in treatment weeks 2 and 5. Normal sample distribution was confirmed with Shapiro-Wilk test. Unpaired t-test analysis of the mean SUVmax(tumor)/SUVmean(muscle) ratios of F-MISO-PET in weeks 0, 2 and 5 were performed. Significance-level was defined as p<0.005.

**Results:** Between 2012 and 2014 18 patients (16 men, two women, mean age 60 years), treated for HNSCC with dRCTx were included. All received a total dose of 70 Gy in 35 fractions. Concomitant cisplatin chemotherapy was administered in weeks 1, 4 and 7. 14 patients had all F-MISO-PET scans, while 4 had two F-MISO-PET scans (week 0, 5). The mean follow-up time was 14.6 months (range: 4 - 28 months). Mean SUVmax(tumor)/SUVmean(muscle) in weeks 0, 2 and 5 were 1,9 (n=18, SD ± 0.1), 1,5 (n=14, SD ± 0.1) and 1,2 (n=18, SD ± 0.1), respectively. Unpaired t-test for SUVmax(tumor)/SUVmean(muscle) between week 0 and 5 was performed, showing a significant decrease (p<0.0001). Between weeks 0 and 2 (p=0.0346) and between weeks 2 and 5 the decrease again was highly significant (p=0.0113). In two patients no residual hypoxia was measured in week two, resulting in SUVmax(tumor)/SUVmean(muscle) =1.0. In week 5 this was found in seven patients. In two patients hypoxia had increased in week 2 but decreased in week 5 compared to pre-treatment measurements. In one patient hypoxia had increased by the end of treatment.

**Conclusion:** Differences in hypoxia between weeks 0-2, 2-5 and 0- 5, respectively, show statistical significance. This is crucial in the process of re-oxygenation. As concluded in previous works, change of treatment strategy, e.g. by means of dose escalation might be most efficient early during treatment. However further analysis, with more patients and correlation to disease-free and overall-survival are needed.

**EP-2060**
**Correlation of imaging data with known predictive/prognostic factors in Oropharyngeal cancer**

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**Purpose or Objective:** There is increasing interest in maximising data extraction from the multimodality imaging performed in cancer patients in order to predict treatment outcomes. This is particularly relevant in Oropharyngeal cancer where concomitant chemoradiotherapy is the standard treatment for stage III and IV disease but there is significant variation in patient outcomes and both treatment intensification and de-intensification strategies are being investigated.

The aim of this prospective pilot study was to look at how data obtained from pre- and per-treatment 18F-FDG-PET/CT scans and textural features from pre- and per-treatment contrast enhanced planning CT scans correlated with known prognostic indicators including smoking history and HPV status.

**Material and Methods:** Eligible patients included those undergoing primary concomitant chemoradiotherapy for Stage III/IV SCC of the Oropharynx. Each patient underwent a contrast enhanced planning CT and an 18F-FDG-PET/CT scan immobilised in the treatment position prior to the start of treatment and then again after 8-10 fractions of radiotherapy. The SUVmax and SUVmean were recorded on both the pre- and per-treatment 18F-FDG-PET/CT. Texture analysis was performed using TexRad software on both the pre- and per-treatment planning CT scans. The smoking history for each patient was established on enrolment to the study and HPV status was determined using p16 IHC on biopsy of the primary tumour. Ethical approval was gained from the relevant bodies.

**Results:** Eighteen patients were recruited. HPV status was positive in 13 patients and negative in 5 patients. The SUVmax/mean in HPV negative patients was 21.6/13.3 on the pre-treatment 18F-FDG-PET/CT versus 15.2/10.5 for HPV positive patients (p<0.09/0.25). Pre-treatment CT texture analysis showed a difference in the normalised entropy between the two groups with a significant difference detected using the smallest filter (p=0.04). The SUVmax/mean on the pre-treatment 18F-FDG-PET/CT for patients with no or minimal smoking history (<10 years) was 13.7/9.5 versus 19.1/12.9 for those with a smoking history of >10years (p< 0.1/0.13). No significant difference in the entropy/entropy ratio between the two groups was detected. No significant differences were shown in the change in SUV or entropy ratio between the pre- and per-treatment scans in any of the groups.

**Conclusion:** These results suggest differences in the imaging characteristics between patients in different prognostic categories may be detected at the pre-treatment stage and are worthy of further investigation in a larger patient cohort and may in the future add further information to that provided by the molecular profiling of tumours. This study did not show any significant differences in the data obtained between patients in terms of their early response to treatment however this data can be revisited once follow up data for this patient cohort matures.

**EP-2061**
**Over-expression of EGFR and/or cox-2 in locally advanced squamous cervical cancer (LASC)**

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**Purpose or Objective:** This study looking for the prognosis value of over-expression of EGFR and/or COX-2 in patients with locally advanced squamous cervical carcinoma (LASC).