showing residual disease on FDG-CT-PET scan 70 days post-treatment, were studied. The volume of residual disease was defined by the area with a Standardized Uptake Value (SUV) higher than mediastinal uptake. Overlap fractions (OF) were calculated between this residual disease volume and the original tumor, with several SUV threshold based auto-delineations on a FDG-CT-PET scan before radiotherapy.

2. Stability of the high FDG-uptake areas during radiotherapy. Twenty-three patients underwent repeated FDG-CT-PET scans before and one and two weeks after the start of radiotherapy. Tumors with volumes >70 cm^3 (n=9) were used to assess heterogeneity in FDG-uptake. OF's were used to demonstrate the stability of the high FDG uptake regions (50% SUV volume) during treatment.

Results: 1. *Location of residual disease within the tumor.* The location of the residual disease was nearly completely (OF > 95%) within the contour of the original tumor, defined as the 34% threshold SUV contour, based on the source-to-background ratio (van Baardwijk *et al* *I*nt J Radiat Oncol Biol Phys, 2007). As depicted in figure 1, on average (bold black line) the residual had an OF of more than 80% with the 50% threshold of the pre-treatment PET scan. This indicates that residual disease occurs within the high-uptake region of the original tumor and therefore, escalating dose to this specific area is likely to improve local control.

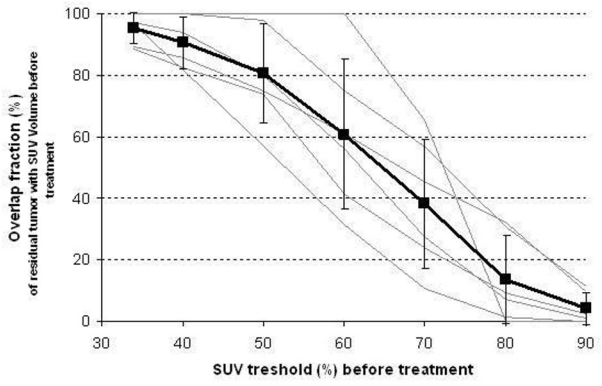

Figure 1. Overlap Fractions of the residual tumor with the SUV threshold of the PET scan before radiotherapy.

2. Stability of the high FDG-uptake areas during radiotherapy The mean OF's of the high uptake zone during therapy were 75.7 ± 10.9% at day 7 and 67.5 ± 16.4% at day 14 during treatment. So, the location of the high FDG uptake region within the tumor during treatment remained the same.

Conclusions: Residual disease within the primary tumor is not due to geographic miss. The location of residual disease corresponds with the original 50% highest FDG uptake before radiotherapy.

This location of the high FDG uptake within the tumor remained stable during radiotherapy. Boosting of tumor sub-volumes may thus be feasible and potentially beneficial, using only a FDG-PET scan before therapy.

D7-06 **Novel therapeutics II, Thu, 12:30 - 14:15**

Open Non-randomised Phase II Pilot Study of Neoadjuvant Cetuximab in combination with Cisplatin and Gemcitabine in patients with resectable Non-small Cell Lung Cancer

Coate, Linda E.; Cuffe, Sinead; McDowell, Dermot; Gately, Kathy; Barr, Martin; Meaney, James; O'Connell, Finbar; Nicholson, Siobhan; Young, Vincent; O'Byrne, Kenneth

St. James' Hospital, Dublin, Ireland

Background: Adjuvant and neoadjuvant chemotherapy play a role in optimising long-term outcome of patients with resectable non-small-cell lung cancer (NSCLC). The epidermal growth factor receptor (EGFR) is a receptor tyrosine kinase that is overexpressed in NSCLC. Cetuximab, a monoclonal antibody, targets the extracellular domain of the EGFR preventing ligand binding. Preclinical data and phase II evidence in advanced NSCLC suggest that cetuximab potentiates the activity of conventional cytotoxic agents.

Methods: Patients with histologically confirmed resectable stage IB-IIIA NSCLC and adequate end-organ function, giving informed written consent were eligible. Patients received 3-weekly cycles of cisplatin 80mg/m^2 d1, gemcitabine 1250mg/m^2 d1 & d8 and cetuximab 400mg/m^2 loading dose, thereafter weekly 250mg/m^2. The primary endpoint is response rate (radiological and pathological). Secondary endpoints are safety and tolerability of the combination, resection rate following therapy, overall survival and relapse free survival. In addition serum, plasma and white blood cells are being collected before, during and after therapy from all patients. For proteomic analysis undenatured and unfractionated pretreatment serum samples underwent Surface Enhanced Laser Desorption/Ionisation Time of Flight Mass Spectrometry (SELDI-TOF MS) profiling using a strong anion exchange ProteinChip® array (Q10 Array).

Results: 30 patients have been recruited to date (19 men, 11 women), median age 64 (range 29-77), 24 patients stage I, 2 patients stage II, 4 patients stage III. 27 patients have completed treatment and are evaluable for response. The overall response rate is 76% including CR - 1 patient, PR -18 patients, SD -7 patients, PD -1 patient. The most common toxicity was skin rash (100%). The commonest grade 3/4 toxicities were neutropenia (52%) and thrombocytopenia (36%). There were 3 grade 3 and 4 grade 4 cardiovascular toxicities in patients with significant co-morbid cardiovascular toxicities including peripheral arterial ischemia (2), cerebrovascular accident (3) and myocardial infarction (2). One patient was withdrawn from study because of complicated peripheral ischemia. Using ciphergen express software serum proteomic analysis in 21 patients divided into two groups -radiological responders vs non-responders - revealed six differentially expressed peaks.

Conclusions: The response rate appears higher then that reported for neoadjuvant chemotherapy in other studies. Patient accrual continues. Ongoing biomarker studies may identify those patients most likely to benefit from induction treatment. In order to maximise the protein peaks we have depleted our samples of IgG and Albumin. We are currently profiling these denatured and depleted samples on three ProteinChip® arrays.