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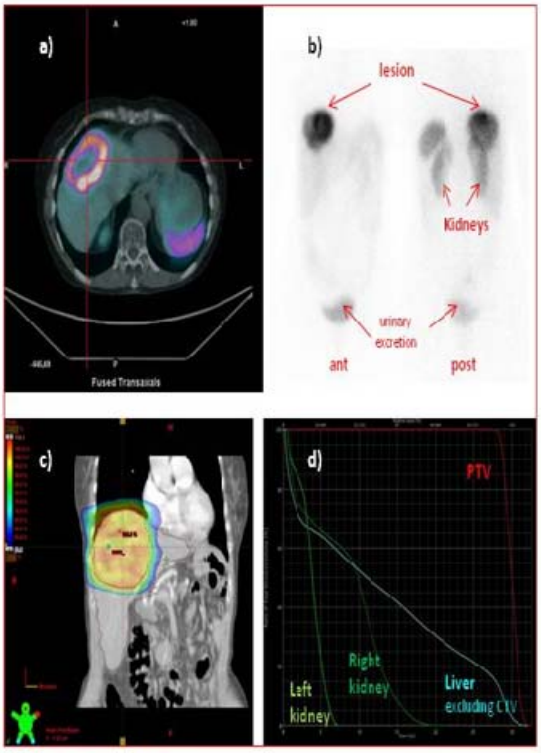
Results: The table reports the median value (range) of administered activities and absorbed doses to OARs for the PRRT as well as doses delivered with ERBRT. T doses for PRRT were very variable inter- and intra-patients (YD: 1-42 Gy/GBq; LuD: 1-56 Gy/GBq).

PRRT			
	YD	LuD	treatment
Administred activity (GBq)	7.4 (2.9-22.8)	21.0 (3.6-40.7)	
Absorbed dose to OARs	(Gy/GBq)	(Gy/GBq)	(Gy)
K	2.7 (1.0-7.8)	0.6 (0.4-1.8)	19.2 (2.3-32.5)
RM	0.07 (0.03-0.14)	0.04 (0.02-0.06)	1.0 (0.2-1.6)
L	0.59(0.10-2.54)	0.05 (0.01-0.09)	1.7 (0.2-13.5)
EBRT			
Prescription dose (Gy)	28.5 (20-45)		
Dose per fraction (Gy)	4.6 (3-15)		

No severe toxicity was observed for RM (7 pts grade II; 7 pts grade I; 3 none); no toxicity was registered for K and L but in one pt (K, grade I). Median follow-up was 3.5 (0.2-12.3) yrs; 7 pts died.



Dosimetry details of pt 8, affected by pancreas NET, treated with 27.9 GBq of LuD. She had a liver met (200 ml) non responding to PRRT, treated afterwards with EDFT (dose: 30 Gy, 10 fractions, RapidArc technique). Mean absorbed doses were: for PRRT, K=17 Gy, RM=1.1 Gy, L=1.4 Gy, clinical target volume (CTV)= 230 Gy; for EBRT: K_{right}= 8.3 Gy, K_{left}= 3.8 Gy, liver excluding CTV=12.8 Gy, CTV=30 Gy. Both treatments were well tolerated (RM grade I, K, L absent). a) fused SPET/CT image (axial) and b) planar whole body (anterior, posterior) images of LuD; c) isodose distribution in a coronal plane; d) DVHs for the target and OARs. The patients is alive after 5 yrs of follow-up.

Conclusions: EBRT is not infrequently proposed in PRRT pts. PRRT and EBRT have generally different OARs and are compatible therapies that can deliver complementary doses to the T without increased toxicity. However, most often EBRT irradiates bone and liver mets, potentially delivering non negligible doses to K, RM, L, once summed to the doses delivered by PRRT (figure d). Dosimetry for combined PRRT and EBRT deserves multidisciplinary discussion, being aware of the large variability of PRRT doses due to individual metabolic behavior. Our results indicate that combined PRRT and EBRT have a great potential and could represent a base for future prospective studies.

Poster: Radiobiology track: Tumour microenvironment, hypoxia and angiogenesis

PO-1065

Impact of fractionated radiotherapy on tumor microenvironment

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Purpose/Objective: Radiotherapy (RT) is used in cancer treatment for more than a century. Over years, the impact of ionizing radiation on isolated cancer cells was extensively studied and the biological mechanisms implied in DNA repair were elucidated. The responsiveness and behavior of cancer cells following RT *in vivo* may drastically differ from what is observed *in vitro*. The impact of the tumor components (i.e. hypoxia) on tumor responsiveness to treatments (e.g. chemotherapy and radiotherapy) is well established. Nevertheless, few studies are focused on the impact of the radiotherapy treatment on the tumor microenvironment and its consequences on cancer progression and metastatic dissemination.

Materials and Methods: With an *in vivo* xenograft model of neoadjuvant RT, we studied the impact of different RT schedules on the tumor microenvironment compared to non-irradiated tumors.Thanks to diverse techniques (RT-PCR, western blot, IHC, FACS), we evaluated the state of different tumor microenvironment components (i.e. MMPs, fibroblasts, vascular density and hypoxia, inflammation and innate immunity, adipocytes) at different timings (4 and 11 days) following RT (5x2Gy and 2x5Gy).

Results: We observed a decrease in tumor vessel density and it is associated with an increased of tumor hypoxia and VEGF-A mRNA levels in the irradiated tumor compared to the non-irradiated controls. Moreover, the study of the innate

immunity showed very different profiles following RT compared to controls. Surprisingly, we observed very little variations between the different RT schedules. We performed FACS analyses on blood and on tumors collected 4 or 11 days following the 2 RT schedules or from non-irradiated mice. In the blood, we observed a net increase of $DX5^+$ NK cells and an important decrease of eosinophil in the irradiated group of mice compared to the non-irradiated mice. Four days after RT treatment, we observed a transient decrease in neutrophil and $Ly6C^{low}$ monocyte and a transient increase in $Ly6C^{high}$ monocyte that return to the level of the non-irradiated group at day 11. Inside the tumor, results showed a drastic decrease in dendritic cells following RT, no significant difference in $F4/80^+$ macrophage proportion between groups, but RT appeared to induce a switch in macrophage polarization with a decrease in $MHCII^{high}$ macrophage (M1) proportion and an increased $MHCII^{low}$ macrophage (M2) proportion.

Conclusions: These data demonstrate that RT profoundly modifies several components of the tumor microenvironment, with minor variations according to the RT schedules. These modifications could impact the behavior of the primary tumor and should be taken into account to avoid tumor dissemination or for improving treatments efficacy.

PO-1066

PET FMISO investigation of head and neck tumor cell lines treated with cetuximab

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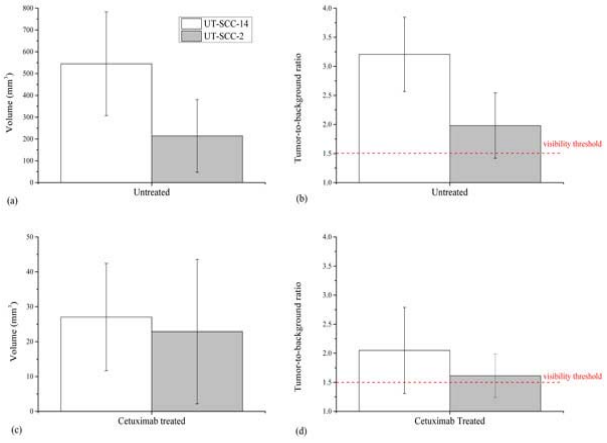
Purpose/Objective: Cetuximab is an inhibitor of the epidermal growth factor receptor (EGFR) impairing the molecular signals for cell division. Cetuximab has been approved for treatment of advanced head and neck tumour squamous cell carcinomas (HNSCC) that are often associated with poor prognosis, resistance to treatments and low 5-year survival rate. The purpose of this study was to investigate correlations between responsiveness to cetuximab treatments and tumour oxygenation in two mouse HNSCC models.

Materials and Methods: Two HNSCC cell lines (UT-SCC-2 and UT-SCC-14) were cultured and injected subcutaneously in BALB/c (nu/nu) nude mice at two sites in each mice (N = 60). UT-SCC-14 is sensitive *in vitro* for cetuximab, while UT-SCC-2 is more resistant *in vitro*. After one week of tumour growth, half of the mice received three cycles of 50mg/kg cetuximab intra-peritoneally (during 9 days) and the others were kept as controls. All the mice were subsequently imaged with ^{18}F-fluoromisonidazole (FMISO) in a Siemens Focus 120 microPET. Volumes of interest in the tumour and background (arm muscle) were manually delineated and the tumour-to-background ratio (T/B) calculated as the mean standard uptake value (SUV) in the considered volumes. Tumours with T/B≤1.5 (visibility threshold) were not discernible from the uptake in the surrounding area.

Results: The results showed a positive correlation between FMISO uptake and tumour size in untreated tumours, with UT-SCC-14 having higher T/B ratios than UT-SCC-2 tumours. In the case of treated tumours, UT-SCC-2 showed FMISO tracer uptake almost at the visibility threshold level, in spite of the similar tumour volumes with UT-SCC-14 that had significantly higher uptake, albeit under the values in untreated tumours. The oxygenation assessed based on PET FMISO of the tumour derived from the cell line *in vitro* resistant to cetuximab, UT-SCC-2, was better than the oxygenation of the tumour based on the sensitive cell line UT-SCC-14 after the treatment with cetuximab.

Conclusions: These results indicating a possible mechanism for cetuximab to influence the oxygenation of tumours may be exploited for maximising the therapeutic gain provided that further investigations are conducted.



PO-1067

Evaluation of on- and offline bioluminescence tomography system for focal irradiation guidance

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Purpose/Objective: Our group has constructed an on-board bioluminescence tomography (BLT)/cone-beam CT (CBCT) guided small animal radiation research platform (SARRP) for preclinical radiation studies. We hypothesize that BLT guidance on-board the SARRP system would provide more accurate radiation guidance than an off-line system by eliminating the need of animal transportation between the optical system and SARRP. However, the on-board BLT system complicates system design, and the necessary workflow sequence of BLT, CBCT and irradiation is likely to result in low experimental throughput as compared to an off-line