PO-0913
Efficiency of videofluoroscopy to detect radiotherapy and radiochemotherapy-induced swallowing dysfunction
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Purpose/Objective: Head and neck cancer treatment is associated with significant morbidity. Both exclusive radiotherapy (RT) and chemoradiotherapy (CRT) treatments can produce, as side effects, impairments of swallowing, long-term dysphagia. The aim of the study here presented was to evaluate the ability of videofluoroscopy (VDF) in detecting and measuring swallowing dysfunction secondary to treatments.

Materials and Methods: Eight head-and-neck cancer patients, who underwent radical RT till 70 Gy (5 fractions per week, 2 Gy per fraction), and concurrent chemotherapy (CHT) when indicated, were included. Treatment schedules administered to each patient (RT total dose, radiation fields, delivery techniques, CHT schemes) were decided according the NCCN recommendations. Half of patients received exclusive RT and the other half concomitant CHRT.

In order to evaluate a possible swallowing dysfunction, VDF were performed before and after the treatment. Patients presenting swallowing dysfunction before the treatment were excluded. Post-treatment evaluation was undertaken twice: early (1-3 months) and late post-therapy (4-9 months). The VDF explored swallowing dysfunction with the standard different textures.

Results: Three patients developed swallowing dysfunction in early on post-therapy evaluation and, in the late post-therapy evaluation, 7 patients showed propulsive defect of the pharynx and 6 of them had also residue. Only one patient had symptoms related to this dysfunction. No case of pneumonia by aspiration was reported.

Conclusions: Swallowing dysfunction is a prevalent side effect after intensive RT and CHRT treatment in head-and-neck cancer patients. In our first 8 patients included, most frequent swallowing dysfunction was the propulsive defect of the pharynx asymptomatic in most of the cases. VDF was very effective in detecting, measuring and controlling this side effect. However, in order to confirm these results, inclusion of more patients is required. Therefore, patient enrolment continues.

PO-0914
Quantitative assessment of acute skin erythema and pigmentation due to breast radiation using spectrophotometry
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Purpose/Objective: In daily clinical practice, acute adverse skin reactions due to radiation therapy (RT) are graded by the experienced eye of the radiation oncologist. However, such subjective grading provides only rough estimates of RT response. In addition, a great range of skin reactions is observed even between patients undergoing the same treatment. Aim of our study was to implement a quantitative method, based on reflectance spectrophotometry (RS), for objective in vivo measurements of skin erythema and pigmentation due to RT. Correlations between RS measurements and both clinicians’ skin toxicity perceptions and delivered superficial doses were investigated.

Materials and Methods: Patients treated with tangential fields to the breast parenchyma were included. RT prescribed dose: 50-60Gy, 2Gy per fraction. Skin RS measurements were obtained by means of a commercially available system (SpectroShade, MHT) which allows to acquire skin reflectance data between 483 and 950nm inside an useful field of view of 18x14mm². Measurements were performed before RT and approximately every 6 (range 4-8) RT fractions up to the end of the RT treatment. At the same time, skin acute toxicity grade (ATG) reactions were visually assessed and recorded by the physician using RTOG scoring system. Both instrumental RS measurement and subjective ATG were performed at five different fixed points within the field of view treated with RT. RS relative changes at two selected band widths centred at 560nm (haemoglobin absorption peak) and 720nm (mainly melanin absorption) were analysed and their correlation with ATG and delivered superficial dose was investigated.

Results: Preliminary analysis of measurements at inframammary fold on 11 pts is here presented. Skin RS relative changes at 560nm (RS560nm) were a strong indicator of skin erythema and correlated well with clinical ATG evaluation (fig 1a). No evidence of a relationship between superficial absorbed doses (at inframammary fold) and RS560nm was obtained. However, after an initial 30Gy irradiation, where patient-to-patient variability to RT resulted to be extremely high, RS560nm data clearly indicate the existence of 3 different groups of patients, i.e. over-normal- and under-reacting to RT, with RS560nm values <0.6 (3pts), in 0.8-0.9 range (6pts) and >1.1 (2pts), respectively (fig 1b). Finally, skin RS relative changes at 720nm (RS720nm) resulted to be mostly related to skin pigmentation and started to slightly modify at the very end of the RT.

Figure 1: (a) correlation between skin acute toxicity grade (ATG) evaluations and reflectance spectrophotometry relative changes measurements centred at 560nm (RS560nm); (b) relative skin reflectance (560nm) as a function of dose to the inframammary fold for the 11 considered patients.

Conclusions: RS is a good and objective tool to evaluate skin erythema and pigmentation changes. Although preliminary, these data are very interesting and do deserve further investigation. More patients will be recruited to investigate the origin of the variation in patients radiosensitivity, possibly the genetic level. This study was funded by a grant of Mrs M. Bonatti and Mr G. Mameli and by the National Cancer League
significantly upregulated on day 2 after 4 Gy in vitro irradiation in both groups (approximately 6-fold in controls and 2.5-fold in cases), but appears to decay more slowly in fibroblasts from cases. However, cases show a significantly higher level of p53 than controls (p=0.0025) and this effect independent of any further radiation exposure.

Conclusions: DNA damage, in particular unrepaird DSB is not a significant factor in the development of late breast fibrosis after radiotherapy.

POSTER: PREVENT TRACK: FUNCTIONAL IMAGING OF NORMAL TISSUE DOSE RESPONSE

PO-0916

Relations between increased SUVmax in esophagus during radiotherapy treatment and dysphagia.

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Purpose/Objective: To validate the hypothesis that: a) The increase of esophagus SUVmax one week after the start of radiotherapy treatment is correlated with parallel severe dysphagia grade (≥ 2), and b) The increase of esophagus SUVmax at one specific level is correlated to the dose given at this specific level and c) To investigate whether some specific anatomical regions of the esophagus (divided into 3 equal parts) are more sensitive to inflammation than others.

Materials and Methods: A cohort of 39 non-small cell lung cancer patients treated with curative intent and having had two FDG PET scans: one before treatment and approximately one week after start of treatment (average 9 ± 2 days). Dysphagia toxicity, PET and CT scans were analyzed for each patient. The esophagus has been divided into 3 equal regions: a caudal region (part 1), a middle region (part 2) and a cranial region (part 3).

The maximal PET-SUV value in the esophagus (SUVmax) was computed, excluding the GTV regions, for the whole esophagus and for each part of the esophagus on both time points. The change in SUVmax, ΔSUVmax, was calculated. This change was correlated to the incidence of severe dysphagia (grade ≥2).

The patients were divided into 2 groups: one group (Gr 2) consisted of patients with dysphagia toxicity larger than grade 2 and the other group (Gr 1) contained patients with mild or no dysphagia (grade 0 or 1). The average difference of SUVmax is measured for each of the groups, ΔSUVmax.

-The dose was computed for each esophageal region. We then correlated the dose given to each third to the ΔSUVmax on the corresponding region.

Results: The dose delivered to the patients until the second PET/CT scan was on average 2.1 ± 3 Gy.

-The increase in SUVmax was significantly higher in the severe dysphagia group (ΔSUVmax = 0.34 ± 0.66 of increase in Gr 2) than for patients without dysphagia toxicity (0.17 ± 2.1). By using the one-sided Wilcoxon rank sum test, the p-value was significant (p=0.055).

-Increase in SUVmax was highest in the most cranial part of the esophagus for the patients having severe dysphagia: ΔSUVmax = 0.53 ± 0.81 compared to the patients without toxicity: ΔSUVmax = 0.18 ± 1.3, with a trend towards significance (p-value =0.06).

-The increase in SUVmax for the middle and cranial parts were not significant (large p-values > 0.20).

Conclusions: Significant increase in SUVmax for patients with severe dysphagia was observed. The increase in the caudal third of the esophagus was higher for patients with severe dysphagia compared to the other parts of the esophagus. A validation study or an extension of the cohort patients is however necessary.

Figure 1. Summary showing for each part of the esophagus the difference of ΔSUVmax for each region of the esophagus: its value (of increase), standard deviation, p-value and significance of the one-sided Wilcoxon rank sum test.

POSTER: PREVENT TRACK: BIOLOGICAL EFFECT OF NEW IRRADIATION MODALITIES

PO-0917

Radiobiological aspects of intraoperative radiotherapy with large dose fractions.

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Purpose/Objective: Novel radiotherapy techniques such as stereotactic radiosurgery (SRS), stereotactic body radiation therapy (SBRT), high-dose-rate (HDR), brachytherapy boost, and intraoperative radiotherapy (IORT), use a single or very few, very high dose fractions. Furthermore, the total time required to apply a dose fraction may be increased, allowing induction and repair of sublethal lesions during the treatment. In addition, IORT potentially influences subsequent wound healing. This departure from conventional fractionated radiotherapy may influence the biological effect in several ways. The purpose was to study the influence of high single doses, and protracted irradiation, on RBE, repair, and wound healing in vivo.

Materials and Methods: Human MCF7 breast cancer cells, normal skin fibroblasts and endothelial cells (HUVEC), and hamster V79 cells, were used. Irradiation was performed with 50 kV X-rays from the Intrabeam® machine with a 4 cm applicator for tumour-bed irradiation (Carl Zeiss Surgical, Oberkochen, Germany) or 6 MV X-rays from a linear accelerator. Clonogenic cell survival was determined by the colony formation assay; repair halftimes of sublethal damage (SLD) were determined from split-dose experiments; DNA double-strand breaks (DSB) were monitored by phosphorylated histone H2AX foci; cell migration was quantified by the in vitro wound healing (scratch) assay.

Results: The RBE of 50 kV X-rays was increased relative to 6 MV (mean 1.35; 95% c.i.:1.21-1.5) at a dose rate in a water-equivalent tumour phantom (dose rate 15.1 Gy/min) but a decrease with increasing dose as predicted by the linear-quadratic (L-Q) formalism was not observed. However, RBE was decreased irrespective of dose at the lower dose rate of 9.8 Gy/min in 12.7 mm depth. This could be partly explained by continuous induction and repair of SLD during protracted irradiation. On the other hand, residual H2AX foci in V79 cells 24h after irradiation with 4.7 Gy (equivalent to approximately 6 Gy of 6 MV X-rays) decreased with decreasing dose rate (23 to 7 Gy/min) in air, indicating a possible limiting role of the DSB repair system. Whereas a dose of 12 Gy of 6 MV X-rays strongly inactivated fibroblast colony formation, migration in the wound healing assay was not inhibited, and even slightly stimulated, by irradiation. The cytokine TGF-β1, which plays a central role in wound healing, inhibited migration but no interaction between irradiation and TGF-β1 was observed.

Conclusions: The RBE, and effects of repair during protracted dose delivery, should be taken into account when assessing biological effects of large dose fractions of IORT. However, deviations from the dose dependence predicted by the L-Q formalism were observed. Unexpectedly, no adverse effect of high-dose irradiation on migration was observed in the absence or presence of TGF-β1. Further studies of the biological effects of very large dose fractions are warranted.

PO-0918

Effects of everyday low-dose pre-irradiation followed by high dose on cancer and normal cells in vitro

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Purpose/Objective: The effects of radio-adaptive response is the main interest in many studies. The exposure of cell lines to low-dose irradiation leads to changes at molecular level which may induce adaptive response. Cells and tissues exposure to low doses followed by higher irradiation doses is named radioadaptive irradiation. Adaptive response can lead to hypersensitivity or radioresistance. The aim of this research was to examine the effects of everyday low-dose pre-irradiation on cell viability in two cell lines: cancer cells and fetal lung fibroblasts.

Materials and Methods: We studied the effect of a low-dose pre-irradiation (0.03Gy, 0.05Gy and 0.07 Gy), applied everyday solely and also everyday prior to 2.0Gy challenging dose after two hours, on