Results: Irradiation with low doses enhanced the motility of the cells. Slit2 as well as Robo1 was extremely low expressed in the cell line with higher motility (U87). Irradiation reduced the expression even more. On the other hand, a stable overexpression of Robo1 decreased significantly the migration of the cells and suppressed the increase in motility observed after irradiation. In contrast, the siRNA mediated knockdown of Robo1 increased the migratory potential of the cells. The analysis of FAK, a key player in cellular migration, revealed a decreased expression in Robo1-overexpressing cells.

Conclusion: Our data indicate a role for Robo1 in the migration of malignant GBM cells. The expression of Robo1 reduced the migration of these cells and was also able to impede the increase in motility observed after irradiation with photons.

Poster: Radiobiology track: Radiobiology of protons and heavy ions

PO-0999

Reduced side effects by proton minibeam radiotherapy in a mouse ear model

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Purpose or Objective: Proton minibeam radiotherapy aims to minimize normal tissue damage in the entrance channel while keeping tumor control through a homogeneous tumor dose due to channel widening with increasing track length. Side effects of proton minibeam irradiation were examined in an in-vivo mouse model to account for immune system, vasculature and higher complexity. Here, we report on our comparative study of minibeam and broad beam irradiation in the ear of Balb/c mice, to prove this hypothesis of reduced adverse effects in normal tissue.

Material and Methods: At the ion microprobe SNAKE, 20 MeV protons were administered to the right ear of 2-3 months old, female Balb/c mice, using an average dose of 60 Gy in a field of 7.2 x 7.2 mm2 in the central part of the ear, in two irradiation modes, homogeneous and minibeams. The 4 x 4 minibeams of 180 x 180 µm2 size were set in a distance of 1.8 mm, resulting in a dose of 6000 Gy in the channels, but with negligible dose in between. Inflammatory response, i.e. ear swelling and skin reactions were monitored for 90 days following irradiation, as well as genetic damage and release of inflammatory proteins.

Results: No ear swelling or other skin reaction was detected after the minibeam irradiations, while significant ear swelling (up to 4-fold), erythema and desquamation (crust formation) developed in homogeneously irradiated ears 3-4 weeks after irradiation. Loss of hair follicles was only detected in the homogeneously irradiated fields after 4-5 weeks.

Conclusion: Our results prove that proton minibeam radiotherapy leads to reduced side effects compared to conventional broad beam irradiation and could become an option in clinical proton and/or heavy ion therapy.
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PO-1000

Effect of X-rays and carbon ions on cell survival and expression of Hh pathway genes in cancer cells

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Purpose or Objective: Metastasis is an important cause of mortality in cancer patients and evidence shows that irradiation could actually increase the formation of metastasizing cells. An important pathway implicated in the process of metastasis is the Hedgehog (Hh) signaling pathway. Recent studies demonstrated that activation of this pathway can lead to radioresistance. So far, the impact of high-LET radiation on the Hh pathway is still unknown. In the present study the impact of different radiation qualities (e.g. X-rays and carbon ions) on Hh gene expression was investigated in prostate cancer cells (PC3) and medulloblastoma cells (DAOY).

Material and Methods: *In vitro* models used for prostate cancer and medulloblastoma were PC3 and DAOY, respectively. Colony survival assays were performed to analyze the effect of radiation on cell survival. The impact of radiation on the expression of the different Hh signaling pathway components (SHH, PTCH, SMO, GLI1, GLI2, GLI3 and SUFU) was investigated by means of RT-qPCR. Experiments with X-rays were performed at SCK•CEN (Mol, Belgium) whereas carbon ion irradiation (LET = 33.7 KeV/µm) experiments were performed at the Grand Accélérateur National d'Ions Lourds (GANIL) (Caen, France).

Results: Colony survival assays showed that DAOY cells were more radioresistant than PC3 cells (respectively D10=5.3 Gy and D10=4.2 Gy). Evaluation of the Hh signaling pathway showed that basal gene expression is present in both PC3 and DAOY, although very low. However, basal gene expression of the Hh components differed between both cell lines. Moreover, the more radioresistant cell line DAOY had higher expression levels of Gli1 compared to the PC3 cells. Preliminary RT-qPCR results show that different radiation qualities induce different changes in the expression of the Hh signaling components.

Conclusion: In conclusion, radiation exposure can induce changes in the Hh pathway. Future experiments will address whether modulation of the Hh pathway also affects the radio-responsiveness of cancer cells.

Poster: RTT track: Strategies for treatment planning

PO-1001

Dosimetric impact of flattening filter and flattening filter-free beams on IMRT planning of NSCLC

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Purpose or Objective: This retrospective study aimed to compare and determine the potential dosimetric benefits of intensity-modulated radiotherapy (IMRT) treatment plans with (FF) and without flattening filter (FFF) as well as to explore the dosimetric differences in 6MV FFF and 10MV FFF plans for non-small-cell lung carcinoma (NSCLC).

Material and Methods: Ten cases of CT data were selected from NSCLC patients. 4 sets of 5-field-IMRT plans were computed with FFF beams (X6FFF, X10FFF) and flattened beams (X6FF, X10FF) with the prescription of total 60Gy in 30 fractions. Planning constraints were based on the Radiation

Therapy Oncology Group (RTOG) protocol 1306. Determination of isocentre, beam arrangement and dose constraints were kept constant in each case. All plans were computed using Varian Eclipse version 11.0 treatment planning system. The plans were then evaluated based on the target coverage, homogeneity, conformity, number of monitor units (MU) to be delivered and dose-volume constraints for various organs at risk (OARs).

Results: All plans exhibited comparable PTV homogeneity (HI ≤ 7.5) and conformity (CI > 96%) with a steep dose fall-off outside the PTVs but at the expense of increased MUs by 39.4% (p=0.007) and 44.7% (p=0.005) for FFF beams at 6 MV and 10 MV respectively. FFF beams offered better dose sparing of OARs than flattened beams. Spinal cord+5mm and volume of 'whole lung (WL) – Gross tumour volume (GTV)' (WL-GTV) that received 20Gy (V20) were reduced by 2% (p=0.017) and 2.8% (p=0.016) respectively in X10FFF plans when compared with X10FF plans. There was also a 16.4 % dose reduction to brachial plexus in X10FFF plans than X6FFF plans.

Conclusion: The application of FFF IMRT for NSCLC yielded quantitatively comparable dosimetric distribution with better sparing of the OARs including 'spinal cord+5mm', V20 of 'WL-GTV' and brachial plexus than using FF beams.

PO-1002

A comparison of outcomes using VMAT and 3DCRT in treatment of esophageal cancer

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Purpose or Objective: There are few studies comparing 3-dimensional conformal radiation therapy (3DCRT) and volumetric modulated arc therapy (VMAT) in treatment of esophageal cancer. These studies often compare 3DCRT unsophisticated, with few treatment beams, which is not common in clinical practice.
Our aim was to compare a modern 3DCRT plan with VMAT using dose volume histograms (DVH) and evaluate the dosimetric profile.

Material and Methods: We evaluate 7 patients with esophageal cancer (4 medium, 2 distal and 1 upper neoplasms). All were contoured using PET-CT and treated with radio-chemotherapy. Target volumes for primary lesions (50-50,4 Gy) and electively treated regions (45 Gy) were contoured.
Every patient had 2 dose-plans, one with 3DCRT (8-10 beams) and other with VMAT (2 arcs) techniques. For each technique, we evaluate the coverage target, homogeneity index of PTV (HI), conformity index (CI), monitor units and DVH metrics of lungs, heart and spinal cord.

Results: VMAT plans reduced total lung volume treated above 20 Gy (V20) and mean lung dose (MLD), but volume treated above 5 Gy (V5) were higher than 3DCRT. VMAT improved total heart volume treated above 20 Gy and 40 Gy (V20, V40) and maximum dose to cord.
Monitor units (MU) were higher with the 3DCRT. HI and CI are better with VMAT technique. Coverage target was very high with both schemes. Statistically meaningful differences were observed (Table 1).

Conclusion: Our results suggest that VMAT for radical treatment of esophageal cancer is useful for decreasing dose in organs at risk. It can play a more important role in some locations, such as cervical cancer. Nevertheless, VMAT increases low-doses in lung and this may contribute increase pulmonary complications.
A complex multibeam technique -3DCRT preserves constraint of organs at risk with high conformity and homogeneity of the target.

		3DCRT	VMAT	p-value
Target	Coverage (%)	98,1 ± 1,4	95,4 ± 1,1	< 0,05
	HI	0,083 ± 0,016	0,047 ± 0,006	< 0,05
	CI	1,62 ± 0,15	1,00 ± 0,03	< 0,05
Lung	V5 (%)	80,5 ± 11,0	83,9 ± 12,0	< 0,05
	V20 (%)	24,5 ± 4,9	14,5 ± 10,0	< 0,05
	MLD (Gy)	15,03 ± 2,13	12,78 ± 2,72	< 0,05
Heart	V20 (%)	48,8 ± 23,2	28,2 ± 22,6	< 0,05
	V40 (%)	16,4 ± 15,8	3,7 ± 4,1	< 0,05
Spinal cord	Maximum dose (Gy)	40,2 ± 3,7	33,0 ± 4,1	< 0,05
	1 cm^3 dose (Gy)	36,3 ± 4,6	30,1 ± 3,6	< 0,05
Monitor units		588 ± 98	558 ± 127	0,499

PO-1003

Does level of DIBH amplitude correlate to reduction in cardiac dose in left breast cancer patients?

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Purpose or Objective: The aim was to investigate whether the amplitude level achieved during DIBH impacted on the mean cardiac dose and V30 reduction in 30 women treated for a left sided breast cancer during radiotherapy.

Material and Methods: Patients were dual scanned in free breathing and DIBH. Varian Real-time Position Management (RPM) was used to record and monitor breathing. Plans were virtually simulated with field borders following IMPORT high guidelines. Pinnacle treatment planning software was used for dosimetric calculation; all plans conformed to ICRU 62. Spearman's Rank correlation and statistical analysis was performed using SPSS v22. All patient data was annonymised. To improve reliability and assess validity of the researcher, 10 of the 30 patients were chosen at random, re-outlined and re-planned to confirm consistency and intra-rater reliability. The heart was also re-contoured for one patient 5 times to calculate the error in heart contouring.

Results: All patients achieved decreased cardiac V30 and mean cardiac dose reduction using DIBH technique. Moderate positive correlation between DIBH amplitude and cardiac V30 reduction was statistically significant (p=0.007, R=0.48). Ratio increase from free breathing to DIBH and cardiac V30 reduction was also positively correlated and statistically significant (p=0.04, R=0.38). Twenty seven percent of patients achieved full cardiac V30 reduction and 73% of patients achieved over 90% reduction. Ratio of amplitude increase from free breathing to DIBH ranged from 4-27 times with ratios of at least 15 times free breathing all achieving 100% cardiac V30 reduction. However 100% cardiac V30 reduction was observed with amplitude of ratio increase as low as 6.25 times free breathing.
Positive correlation between DIBH amplitude and mean cardiac dose reduction was statistically significant (p=0.003, R=0.523). Seventy seven percent of patients achieved over 50% mean cardiac dose reduction with DIBH amplitudes of 1.04-5.46cm. Correlation of ratio of amplitude increase from free breathing to DIBH and mean cardiac dose reduction was not statistically significant (p=0.316, R=0.189).

Conclusion: A 100% reduction in cardiac V30 can be achieved with a DIBH amplitude increase 15 times free breathing, yet full reduction can also be achieved at much lower levels (6.25 times free breathing in the current study) suggesting patients unable to achieve a large amplitude increase may