Imaging with [11C]-metformin in tumor bearing mice showed a large uptake in the kidneys and excretion through the bladder, as expected for metformin. An uptake of [11C]-metformin was seen in both A549 (lung) and SiHa (cervix) tumors and autoradiography supported this finding. Biodistribution of metformin in humans is shown in figure 1 with visible uptake in liver, kidney and the salivary glands, but no detectable uptake in brain, muscle or adipose tissue.

Conclusion: It is possible to visualize distribution of [11C]-metformin in vivo. In xenograft models uptake in tumor was seen. It will be of great interest to investigate whether it is possible to visualize an uptake in human tumors, which will be done in a planned study in prostate cancer patients.

Conclusion: RT increased the levels of OPN expression in GBM tumour cells. This may be a direct effect or related to RT-induced changes in the hypoxic tumour microenvironment that were not detectable on a DCE-MRI or by Glut-1 expression. Although RT significantly increases overall survival compared with surgery alone, particularly when combined with temozolomide, it may promote the cancer stem cell-like phenotype of residual GBM cells. Enhanced OPN/CD44 signaling in the perivascular niche is associated with resistance to therapy and blockade of this signaling pathway may prove of clinical benefit. The relative lack of induction of OPN expression in rectum cancer may explain the success of short course pre-operative RT in this tumour type.

PO-0996
Distinct radiation responses after mtDNA depletion are potentially related to oxidative stress
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Purpose or Objective: In process like reactive oxygen production and apoptosis mitochondria play an important role and both processes play also a significant role in radiotherapy (RT) response. Repair of RT induced damage is dependent on mitochondrial energy supply suggesting a role for mitochondrial DNA (mtDNA) in RT. mtDNA variations, such as mutations or depletion, might therefore influence RT response, as for example found in cisplatin-treated patients. Therefore carefully elucidating the effect of these processes in radiation response might be important. Hence, we hypothesize that reduced mitochondrial function enhances the radiation response as a consequence of reduced ATP production and increased cellular ROS exposure (Fig.1).

Poster: Radiobiology track: Cellular radiation response
PO-0995
Osteopontin expression in glioblastoma - a promoter of the cancer stem cell-like phenotype?
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Purpose or Objective: A high level of circulating osteopontin (OPN) at the end of radiotherapy (RT) is an adverse prognostic factor in patients with glioblastoma (GBM) and other tumours including rectum cancer. Recent mechanistic studies demonstrated Hif2α-mediated OPN/CD44 promotion of the glioma stem cell-like phenotype in a mouse model. Using unique paired tumour samples from patients with GBM, we investigated changes in levels of OPN protein expression following RT and compared these with rectum cancers from patients irradiated with the same pre-operative fractionation.

Material and Methods: 3 patients with histologically confirmed GBM received pre-operative RT in an ethics-approved Phase I trial. 2.5 Gy b.d. was delivered using IMRT over 5 days. Maximal safe tumour resection was performed at 3, 5 and 10 days post RT in patients 1, 2 and 3 respectively. Immunohistochemistry was performed on the paired diagnostic biopsy and irradiated resection specimen using validated antibodies (rabbit polyclonal antibody to OPN: clone PA1-38332, Thermo Fisher Scientific) and an automated immunostainer. The staining was scored by a board-certified pathologist.

Results: Levels of OPN in GBM tumour cells were high at baseline as compared with rectum adenocarcinoma. There was marked increase in OPN expression in response to RT in all three GBM tumours (Fig 1). Expression of Glut-1, a marker of intrinsic hypoxia and a target of HIF-2α, was not induced. Ki67 levels were reduced although levels of cyclin D1 were unchanged. A dynamic contrast-enhanced (DCE) MRI performed on the last day of RT did not detect any change in tumour perfusion in any of the GBMs. Resection specimens from 3 rectum cancer patients irradiated preoperatively with the same schedule showed very low level induction of OPN.

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PO-0996
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Purpose or Objective: In process like reactive oxygen production and apoptosis mitochondria play an important role and both processes play also a significant role in radiotherapy (RT) response. Repair of RT induced damage is dependent on mitochondrial energy supply suggesting a role for mitochondrial DNA (mtDNA) in RT. mtDNA variations, such as mutations or depletion, might therefore influence RT response, as for example found in cisplatin-treated patients. Therefore carefully elucidating the effect of these processes in radiation response might be important. Hence, we hypothesize that reduced mitochondrial function enhances the radiation response as a consequence of reduced ATP production and increased cellular ROS exposure (Fig.1).