Material and Methods: Cell proliferation analysis was performed on human fibrosarcoma, liposarcoma, leiomyosarcoma and rhabdomyosarcoma cell lines with increasing doses of olaparib (0.25; 0.5; 1; 2; 4 µM) 3 h after cells seeding. The numbers of cells were assessed after 5 days and results normalized to the untreated control. For clonogenic assays, fibrosarcoma, liposarcoma, leiomyosarcoma and rhabdomyosarcoma cells were irradiated with 2, 4 or 6 Gy, with or without olaparib (1 µM) iniparib (10 µM) or veliparib (5 µM) pre-treatment. The plating efficiency of the combined treatments were normalized to PARPi- treated cells. The linear-quadratic survival expression was fitted to the data by nonlinear regression. The radiosensitization enhancement ratio for the PARPi at 50% survival (ERS0) was as follows: ERS0 = Dose at 50% survival without PARPi/Dose at 50% survival with PARPi. The impact of PARP inhibition on the survival curve of transplanted tumors treated with olaparib at 1 µM was evaluated in rhabdomyosarcoma cell lines treated with olaparib 1 µM after 48 h, and irradiated at 4 Gy. Cells were probed with primary antibody to v-H2AX.

Results: Continuous treatment with olaparib for 5 days resulted in a dose-dependent inhibition of proliferation in all the STS cell lines. Significant radiosensitization was observed in all human STS cell lines using PARPi, with an ERS0 ranging from 1.2 to 3.41. Rhabdomyosarcoma showed the greatest increase in radiosensitivity, with an ERS0 of 3.41 with veliparib. Fibrosarcoma showed an ERS0 of 2.29 with olaparib and 2.21 with veliparib. Leiomyosarcoma and liposarcoma showed similar radiation responses after PARPi inhibition, with the higher radiosensitization in presence of veliparib (ERS0 1.62 and 1.46, respectively). The combination of olaparib and radiation in rhabdomyosarcoma cells resulted in an increased number of yH2AX foci as compared to control and irradiation alone.

Conclusion: We demonstrated that PARPi are potent radiosensitizers on human STS in vitro models. The different PARPi radiosensitizing effects observed in various cell lines may be explained by the presence of different genomic aberrations in DNA repair machinery in specific STS subtypes. These preliminary data encourage to further study association of PARPi with IR as a promising treatment for STS.

EP-2027
Fractionated radiotherapy plus anti-angiogenic therapy in an orthotopic glioma transplantation model
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Purpose or Objective: Glioblastoma (GBM) is the most common primary brain tumor in adults. Despite intense treatment, including surgery and radiochemotherapy, prognosis is dismal with a median overall survival time of only 15 months. The vascular endothelial growth factor-A (VEGF-A) has been identified as one of the key regulators of neoangiogenesis in these highly vascularized tumors. Therefore, disruption of the VEGF-A signaling cascade by neutralizing VEGF-A and preventing ligation of its receptors appeared to be a promising approach for targeting neoangiogenesis. However, in recent phase III trials application of the VEGF-A blocking antibody bevacizumab in combination with radiochemotherapy failed to prolong overall survival in newly diagnosed GBM despite increasing progression-free survival and improving performance status. The aim of our study was to analyze the treatment effects of radiotherapy in combination with bevacizumab in a clinically relevant setting. Therefore, we established an orthotopic, syngeneic mouse glioblastoma model and subjected it to fractionated radiotherapy in combination with the bevacizumab mouse analogue G6-31.

Material and Methods: GL261 mouse GBM cells were stereotactically transplanted into the frontal lobe of C57/BL6 mice and tumors were allowed to grow for one week. Radiation therapy was performed with a Small Animal Radiation Research Platform (SARRP, Xstrahl) which incorporates contrast agent-CT (CA-CT)-based imaging followed by high precision radiation delivery. Fractionated irradiation with daily doses of 2 Gy up to a cumulative dose of 20 Gy was administered with or without accompanying VEGF-A blockade by the mouse bevacizumab analogue G6-31. Overall survival and tumor size were monitored, histological analyses, and transcriptomic profiling of tumor and normal tissue are currently being performed.

Results: Stereotactic implantation of GBM was successfully accomplished, fractionated irradiation was implemented by CA-CT-based image guidance, and tumor growth was successfully monitored by serial CA-CT scans. The single agent treatments led to a significant delay in tumor growth and prolongation of survival as compared to the sham-treated controls. Importantly, the strongest therapeutic effects were observed with the combined treatment. Histological details, including vessel density and structure, as well as markers of cell death induction, and transcriptomic profiling of tumor and normal tissue are currently under investigation.

Conclusion: This pilot study shows that syngeneic, orthotopic glioblastoma transplants combined with stereotactically delivered radiotherapy are feasible and clinically relevant in vivo models for evaluating the therapeutic efficacy of multimodal treatment approaches based on fractionated irradiation.

EP-2028
Dependence of dose enhancement on the cluster morphology of Gold Nano Particle in radiation therapy
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Purpose or Objective: Injected gold nano particles(GNPs) to a body for dose enhancement are known to form cluster morphology. We investigated the dependence of dose enhancement on the morphology characteristic with an approximated morphology model by using Monte Carlo simulations.

Material and Methods: For MC simulation, TOPAS v.b-12 was used. GNPs of 50 and 100 nm diameter were tested. GNP cluster morphology was approximated as a body centered cubic (BCC) from the center point of the cube. 100 nm GNP at the cube center and calculated the ratio (SER) electrons as a function of distance from the surface of the cluster. For scoring particles, 10 nm width of concentric shell shaped detector was constructed up to 100 nm from the center point of the cube. 10E8 histories of protons and 2 × 10E10 histories of photons were used for simulation. Most values at each detector were summed to obtain the total dose and secondary electrons in a sphere of 100 nm radius and were normalized to 2 × 2 × 2 µm³ cube morphology.