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) oriparib (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 (ER50) was as follows: ER50 = Dose at 50% survival without PARPi/Dose at 50% survival with PARPi. The impact of PARP inhibition on γ-H2Ax foci formation was evaluated in rhabdomyosarcoma cells treated with olaparib 1 µM after 48 h, and irradiated at 4 Gy. Cells were probed with primary antibody to γ-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 ER50 ranging from 1.2 to 3.41. Rhabdomyosarcoma showed the greatest increase in radiosensitivity, with an ER50 of 3.41 with veliparib. Fibrosarcoma showed an ER50 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 (ER50 1.62 and 1.46, respectively). The combination of PARP inhibition on γ-H2Ax foci formation was evaluated in rhabdomyosarcoma cells treated with olaparib 1 µM after 48 h, and irradiated at 4 Gy. Cells were probed with primary antibody to γ-H2AX.

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 V. Albrecht1, J. Schuster1, M. Proescholdt2, D. Pielmaier2, K. Unger3, C. Belka1, M. Niyazi1, K. Laske1, C. Doo Ho Choi2, C. Hee Chul Park2, 1Sungkyunkwan University, Department of Health Sciences and Technology - Samsung Advanced Institute for Health Sciences and Technology, Seoul, Korea Republic of
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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 C57BL/6 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, fractioned 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 synergetic, 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 A. Sang Hee Ahn1, C. Kwangzoo Chung2, H. Younghun Han3, P. Hee Chul Park2, 1Sungkyunkwan University, Department of Health Sciences and Technology - Samsung Advanced Institute for Health Sciences and Technology, Seoul, Korea Republic of
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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 approximate 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 center cubic of 0.25 × 0.25 × 0.25 mm³ (for 100 nm GNP) or 0.18 × 0.18 × 0.18 mm³ (for 50 nm GNP) cube centered at the origin. For scoring particles, 10 nm width of concentric shell shaped detector was constructed up to 200 nm from the center point of the cube. 10E8 histories of protons and 2 × 10E10 histories of photons were used for simulation. Results of the detector 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 mm³ cube morphology.
Results: DER and SER increase as the distance of the GNPs reduces. The largest DER as well as SER was obtained for 0.25 × 0.25 × 0.25 μm³ cube for 100 nm 0.18 × 0.18 × 0.18 μm³ for 50 nm GNPs. In case of 50 nm GNPs, DER increment was 1.421, 1.396, 1.017, and 1.014 for 50 kVp, 100 kVp photons, 70 MeV and 170 MeV protons, respectively. For 70 MeV proton beams, DER was similar to those for 10 MeV, but increment ratio was lower for 150 MeV protons.

Conclusion: As shown in this study, DER with GNPs was larger when they are closely packed in the phantom. Therefore, better therapeutic effects can be expected with close-packed GNPs.

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EP-2029
Feasibility study of Fe3O4/TaOx nano particles as a radiosensitizer for radiation therapy
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Purpose or Objective: To investigate the feasibility of using multifunctional Fe3O4/TaOx (core / shell) nano particles developed for CT and MRI contrast agent as dose enhancing radiosensitizers.

Material and Methods: Firstly, to verify the imaging detectability of Fe3O4/TaOx nano particles, in-vivo tests were conducted. Approximately 600 mg/kg of 9 nm diameter Fe3O4/TaOx nano particles dispersed in phosphate buffered saline (PBS) were injected to ten nude Bab/c mice through the tail vein. Mico-CT (Simens Inveon) was scanned for 5 mice and MRI (BioSpec, 70/20 USR, BRUKER Co.) scan was conducted for rest of mice. For both imaging, 4 consecutive scanning was performed at pre- and post-injection (5 min, 30 min, and 1 hour). Difference between pre- and post-injection images was analyzed by computing the pixel histogram and correlation coefficient factor using MATLAB in the user defined ROI (region of interests). Secondly, to quantify the potential therapeutic enhancement with nano materials, DER (Dose Enhancement Ratio) and number of SER (Secondary Electron Ratio) were computed using MC simulation (TOPAS v.b.12). Diameter of 19 nm circular beams of mono-energetic 10 MeV, 70 MeV, 150 MeV protons were irradiated to a Gold(Au), Tantalum(Ta), TaOx, Fe3O4/TaOx, Fe3O4 nano particle, respectively. For 70 MeV proton beams, DER was similar to those for 10 MeV, but increment ratio was lower for 150 MeV protons.

Conclusion: Fe3O4/TaOx nano particles have potential as a multifunctional agent which enhances the accuracy in cancer detection through visualization of developed tumor lesion and increases the therapeutic effect in proton therapy. The dose enhancement with Fe3O4/TaOx was estimated as half of that of the Gold. However, tumor targeting such as combined with magnetic field may overcome the low DER.

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EP-2030
Gadolinium enhanced x-rays radiotherapy of murine adenocarcinoma Ca755
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Purpose or Objective: The goal of radiotherapy is to deliver into tumor volume certain amount of radiation to kill all tumor cells and at the same time to minimize radiation damage of surrounding healthy tissues. To reach the goal modern conventional radiotherapy uses multifield irradiation with beam changing its shape and intensity. However this approach is not efficient enough in case when healthy and tumor tissues are highly diffused with each other. In this case partial healthy tissues damage is inevitable. Yet another approach is possible. Using some physiological mechanism approach is possible. Using some physiological mechanism one can be able to interact with external radiation more likely than the elements of biological tissues. That leads to dose increase at the site of the element location. For that purpose such elements as iodine, gold etc. and external x-rays radiation(Total energy up to 600 keV can be used). The main obstacle in implementing that method is how to deliver necessary amount of a high atomic number element into a