both radiations. Clustered DNA damage poses serious problems for the DNA repair and error-prone repair of DNA damage is associated with cancer induction. Increased damage complexity following exposure to mixed beams will suggest a higher than expected risk of cancer induction in modern radiotherapy. The results are consistent with the previous studies carried out at SU with different cell types and different biological assays. A synergistic interaction of the beam components was observed at the level of micronuclei, gammaH2AX foci and chromosomal aberrations.

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Angio/lymphangiogenic, inflammatory and immune responses in head and neck cancer: proton vs photon

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Purpose or Objective: Due to its higher precision in tumor targeting, proton therapy could become the treatment of choice for head and neck cancer (HNC). Recent studies have shown that proton irradiation suppresses angiogenic genes and impairs tumor cell invasion/growth. According to the type of radiation, dose and fractionation, the objective of our study was to investigate the effect of proton (P+) versus photon (X) irradiations in squamous cells carcinoma (SCC), in respect of their proliferation, genes expression and proteins secretion involved in proliferation, angio/lymphangogenesis, metastasis and anti-tumor immunity.

Material and Methods: Human SCC CAL33 cells were irradiated 1 to 3 times and evaluated on their proliferation (Cell counting), genes expression (qPCR) for proliferation (TRF2, PLK1), angio/lymphangiogenic (VEGF-A, VEGF-C, VEGF-D) inflammatory (IL6, IL8, CCL2, CXCL12) and immune (PD-L1) responses and protein synthesis (ELISA).

Results: Cell proliferation was evaluated at 48h and at 3 weeks after 1 irradiation and showed a significant decreased in both X and P+, as compared to control but more important in P+. After 3 irradiations, cell proliferation at 48h was reversed and more decreased in X vs P+. Genes expression was investigated at 48h after 1 and 3 irradiations at 2 and 8 Gy. After 1 irradiation, the prevalence of gene expression levels associated with a poor outcome was higher in X than P+ at 8 Gy. After 3 irradiations, genes expression was increased for all but more important for P+ at 8 Gy. The highest expression was noted for VEGF-C (2 to 10 fold increase). The most frequent overexpression was noted for PD-L1, VEGF-C protein induction 48h after 1 and 3 irradiations was increased in both X and P+ groups but decreased in high dose P+, as compared to X.

Conclusion: Cell proliferation activity is in favor of P+ after a single irradiation, and X after multiple irradiations. Genes expression are overall increased in both X and P+, in a dose and fraction dependent manner, implicated in proliferation (TRF2, angio/lymphangiogenic (VEGF-A, VEGF-C, VEGF-D) and immune (PD-L1) responses, VEGF-C protein induction is increased after both X and P+ single and multiple irradiations, but in favor of P+, suggesting a lower lymphangiogenesis/metastatic dissemination immediately after P+. Our study sets the molecular basis for novel therapeutic approaches applicable to HNC in combination with X or P+ radiotherapy, such as angio/lymphangenic inhibitors or immune therapy as anti-PD1 or anti-PD-L1.