Biological dosimetry is defined as the study involving analysis of solid stained dicentric chromosomes and is particularly important because, unlike physical measurement of dose, it takes into account inter individual variation in susceptibility to radiation. The current study is a Hospital based descriptive study conducted in the Department of Radio-therapy, Maulana Azad Medical College and Associated hospitals. 25 diagnosed cases of Head & Neck Squamous Cell Carcinoma were treated by various treatment modalities namely surgery, chemotherapy and radiotherapy alone or in combination. The objective was to quantify the relationship between in vivo chromosome aberration formation and distribution in localized and fractionated radiotherapy in head and neck cancer patients.

Material and Methods

25 patients of Head & neck cancer were irradiated with a daily fraction of 2 Gy, consecutively for 5 days every week for 6-7 weeks in radical/adjuvant settings. Aberrations were measured in these patients by analyzing blood samples taken before starting treatment (day 0), during course of radiotherapy (on day1, day 5, day 15,day 25), at the end of treatment and 6 weeks post treatment. Cultures established in duplicate as per standard protocol using Cytochalasin-B (mycotoxin) for micronuclei & dicentrics separately..

Results

Data was analyzed with one way ANOVA test with Benferroni post-hoc analysis and significant difference was found between mean numbers of Dicentric Chromosome with p value <0.0001 with reference to day 0 as well as between different treatment days which shows that mean frequency ofchromosome aberration increases with increasing radiation dose. However the Nuclear Division index decreases significantly with cumulative doses of radiation. The resulting doseresponse calibration curves with 95% lower and upper confidence limits, pooled from all 25 patients showed a classical linearquadratic shape.

Conclusion

There is a dose dependent increase of chromosomal aberrations, namely dicentric chromosomes and micronuclei in human lymphocytes of head and neck cancer patients undergoing radiotherapy or chemo-radiotherapy.There is a strong impact of the size of the radiotherapy target field on the yield of induced chromosome aberrations. The Nuclear Division Index decreases with increasing dose of radiation beyond 50 Gy. The dicentric is main biomarker for chromosome damage used for cytogenetic biodosimetry as it is known to be almost exclusively radiation-specific with very little difference in the background rate and little inter individual variation. Compared to this, Cytokinesis Block Micronuclei (CBMN) assay has an important advantage of allowing easy and quick analysis however its main disadvantage is related to variable Micronuclei-background frequency. This study demonstrated that induction of dicentric and Micronuclei in human lymphocytes are related in a linear quadratic manner with the irradiation dose. This can prove useful for response assessment and determination of optimum dose of gamma radiation for RT leading to modulation of therapy.

Electronic Poster: Radiobiology track: Radiobiology of prostate cancer

EP-2298 Hypoxia inducible factor 1α confers androgen independence in prostate cancer

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Purpose or Objective

Androgen receptor (AR) and hypoxia inducible factor 1a (HIF1a) are transcription factors that promote prostate cancer progression and radioresistance. This study investigated the relationship between the AR and HIF1a signaling pathways.

Material and Methods

In vitro stable expression of HIF1a was established in the LNCaP cell line by physiological induction or retroviral infection. Tumor xenografts with stable expression of HIF1a were established in castrated and non-castrated mouse models. Gene expression analysis identified transcriptional changes in response to androgen treatment, hypoxia and stable HIF1a expression. The DNA binding sites of AR and HIF were identified using ChIP-seq.

Results

Androgen and HIF1a signaling promoted proliferation and invasion *in vitro* and enhanced tumor growth *in vivo*. The stable expression of HIF1a *in vivo* restored tumor growth in the absence of endogenous androgens. Hypoxia reduced AR binding sites whereas HIF binding sites were increase 11 fold with androgen treatment under hypoxia. TWIST1, KCNN2, PPFIBP2, JAG1, NDRG1 and IGFPBP3 were upregulated both by AR and by HIF1a and showed prognostic significance in at least one of five publically available cohorts.

Conclusion

Overlap between the AR and HIF1a gene expression targets was minimal, indicating that the signaling pathways are mostly independent. Despite the minimal overlap in their gene expression targets, both signaling pathways promoted proliferation and tumor growth. Stable HIF1a expression restored tumor growth and conferred androgen independence. Dual targeting of hypoxia and androgen signaling in combination with radiotherapy is a potential treatment strategy for prostate cancer.

EP-2299 Correlation Of Tcp And Ntcp In Prostate Cancer Patients Treated With High-Dose Radiotherapy

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Purpose or Objective

The advantages of high dose radiotherapy (HdRT) in prostate cancer (PC) have been shown in randomized