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Evaluation of change in blood levels of tumour specific antigens after hypofractionated radiation in head and neck carcinoma

Abstract

Short course hypofractionated radiotherapy is used in palliation of advanced cases of head and neck squamous cell carcinoma (HNSCC). The total radiotherapy (RT) dose used for palliation is usually much lower than the dose used for treatment of less advanced diseases wherein the intent is curative. Still, complete clinical responses are seen in 15 – 30% of such cases. The occurrence of complete responses at such low doses cannot be completely explained by the classical explanation of radiobiology. Radiotherapy exerts its effects on tumours indirectly by generating free radicals that result in DNA damage or directly by DNA double-strand breakage. In addition to DNA damage, radiation causes mitochondrial redox imbalances, lipid peroxidation of cell membranes and a variety of signalling cascades that lead to cells either succumbing to radiation-induced cell death or temporarily arresting cell division to repair the damage. In addition to direct and indirect damage of DNA, RT has been shown to stimulate tumour specific immunity depending on the radiation dose, number of fractions, type of tumour and site of irradiation. RT‘s immune-stimulatory effects take place in many ways, including increased expression of major histocompatibility complex antigens on the tumour cells; release of tumour-associated antigens (TAAs), leading to an in situ vaccine effect; and enhanced expression of immune-stimulatory signals like calreticulin, ATP, heat shock proteins and high mobility group box proteins. RT can also modulate the circulating cytokine profile which may stimulate anti-tumour immunity at distant sites as well. A better understanding of how radiation influences the tumour immune profile will provide insights that will help to optimize strategies for timing and sequencing radiotherapy and various forms of immunotherapy including cancer vaccines, adoptive T cell transfer and checkpoint modulators.

HPV–HNSCC has an intrinsically immune-suppressed tumour micro-environment. Immunotherapy has therefore failed to show durable responses in advanced cases of HNSCC. Evaluating the role of radiotherapy in priming the immune system and tumour micro-environment for immune attack is necessary for creating effective immunotherapeutic strategies. The present project aims to assess the effect of hypo-fractionated radiotherapy in release of tumour associated antigens i.e. MAGE A, NY ESO1 and Brachyury in blood. Peripheral blood samples of 10 consecutive patients of advanced head and neck carcinoma receiving palliative hypo-fractionated radiotherapy will be collected at baseline (before RT) and 1 week after completion of RT. Ten ml of blood from each patient will be collected into a heparinized tube and peripheral blood mononuclear cells (PBMC) will be isolated. PCR will be done to identify MAGE A, NY ESO 1 Antigens.