Purpose: To examine the in vitro gamma-H2AX response in lymphocytes and lymphocyte subsets from patients who have shown severe radiosensitive response (severe late toxicity) in order to determine whether radiation responsive subsets would provide more specific markers for radiosensitivity. To concurrently examine cytogenetic endpoints as potential markers for radiosensitivity in addition to providing additional information about the mechanisms of radiosensitivity.

Methods: Ten prostate cancer patients were identified with grade 3 Late Proctitis (RTOG/EORTC Late Radiation Morbidity Scoring Schema) along with twelve matched normal responding patients (Grade 0 Toxicity). These patients had been treated with dose escalated (76Gy) 3D Conformal Radiotherapy as part of an ongoing Phase III clinical trial. Peripheral blood samples were taken from each patient, irradiated with 250kV, 12.5mA x-rays and examined for gamma-H2AX response in lymphocytes, CD4+ and CD8+ T-cells, and CD19+ B-cells. A dose course experiment was conducted with 6 dose points ranging from 0 to 10 Gy, processed 1 hour after irradiation. The time response of gamma-H2AX was also monitored, with 2 Gy irradiated samples being incubated for 7 time points ranging from 0 to 24 hours before processing. Samples were fixed stained with gamma-HAX-FITC, CD4-PE, CD8-APC and CD19-PC7 before being analyzed by flow cytometry. Furthermore, 0 and 6 Gy irradiated blood samples were analyzed for chromosome aberrations and excess fragments per cell.

Results: In a subset of the data for the radiosensitive population, the gamma-H2AX response tended to be higher in the time course experiment. It was also found that, at 6 Gy, the number of excess fragments per cell in the radiosensitive population (1.65 +/- 0.29) was higher than in the normal population (2.20 +/- 0.27) (p-value < 0.001).

Conclusions: These preliminary results suggest the existence of potential for markers for predicting radiosensitivity which could be useful for tailoring radiotherapy treatments.