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## Biological dose estimation for different photon beam qualities used in radiation oncology

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### Introduction

Although the effect of ionizing radiation in biological systems depends not only on the applied dose, but also on the used energy, dose rate and filters, these parameters are often neglected during radiation therapy. Peripheral blood lymphocytes were irradiated in vitro with a Varian TrueBeam linear accelerator and chromosomal aberrations were analysed in this biological dosimetry study using the linear-quadratic model. Samples were irradiated either with different energy levels or with different dose rates, then dose-response curves were compared. The differences in dose-response effects between gamma photons and kV photons were also studied. Our goal was to identify the potential, substantial variations between different therapeutical scenarios and to explore the limits of the linear-quadratic model.

### Materials and Methods

Venous blood sample was obtained by venipuncture from 22 healthy volunteers into Li-heparinized vacutainers. Blood samples in 2 ml cryotubes were positioned in a water filled plastic phantom in order to achieve homogenous doses. Samples were positioned in the isocenter. Irradiation was conducted with different dose rates as follows: 80, 300, 600 MU/min with 6, 10, 18 MV photon beams and 400, 1600, 2400 MU/min at doses between 0.5 and 8 Gy at room temperature. Flattening Filter free (FFF) mode was also studied at 6 and 10 MV. Metaphases from lymphocyte cultures were prepared by standard cytogenetic techniques: 0.8 ml blood was added to 9 ml RPMI-1640 cell culture medium containing 15 % bovine serum albumin and penicillin/streptomycin (0.5 ml/L). Lymphocyte proliferation was induced with phytohaemagglutinin M (0.2%). Incubation time was 50-52 hours at 37 °C. Cell proliferation was inhibited with 0.1 µg/ml colcemid (Gibco) in the last 2 hours of culturing. Cell cultures were then centrifuged and hypotonized with 0.075 M KCl for 15 minutes at 37 °C, then cells were fixed with cold methanol-acetic acid 3:1 mixture. The cells were dropped on glass slide, and stained with 3% Giemsa. Chromosome analysis was performed in the first cell division, and a minimum of 100 metaphases were scored. All aberration types were recorded: aneuploidy, chromatid and chromosome fragments, exchanges, dicentrics, rings and translocations. Alpha ( $\alpha$ ) and beta ( $\beta$ ) values were calculated for all dose-response curves.

### Results

At lower doses (1-2 Gy) acentrics (not to be confused with the dicentrics or rings coupled fragment) exceeded the number of dicentrics, however, at higher doses this tendency reversed and dicentrics predominated. However, as photon energy increased (at the same dose rate) aberration frequency tended to decrease, i.e. lower energy caused more aberrations. The  $\alpha$  coefficient of dose-response curves was negligibly small, the  $\beta$  quadratic values dominated. The effect of conventional irradiation technique with Flattening filters and intensity modulated radiation therapy mode (FFF) on chromosomal aberrations were also compared. The highest values were as follows: 533 aberrations/100 cells (318 dicentric + ring chromosomes) at 8 Gy, 6 FFF, 400 MU/min. Two Gy dose fractions induced  $14 \pm 0.9$  dicentrics and  $29 \pm 1.6$  all aberrations in 100 cells.

### Conclusion

The effect of 2 Gy dose fractions on chromosomal structure was almost identical at different energy levels and dose rates. However, higher aberration rates were found between the applied modalities when larger fraction doses were used. These results might be important in the case of hypofractionated radiotherapy and radiation incidents.

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