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Abstracts

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PP - 8

Dicentric dose estimates for patients undergoing radiotherapy enrolled in the RTGene study to assess 1) blood dosimetric models and 2) the Bayesian zero-inflated Poisson finite mixture method for estimating partial body gradient exposure.

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Introduction
The RTGene study was focused on the development and validation of new transcriptional biomarkers for prediction of individual radiotherapy (RT) patient responses to ionising radiation. In parallel, for validation purposes, the study has included conventional biomarkers of radiation exposure, i.e. the dicentric assay (DCA) and the γ-H2AX foci assay (FA).

Methods
Peripheral blood samples were taken with ethical approval and informed consent from 20 patients undergoing external beam RT for breast, lung, gastrointestinal or genitourinary tumours. Five samples were taken from each patient: prior to RT, 0.5-2 and 24 hours after the 1st fraction, before the 5th and last fractions. Blood samples were processed using standard methods (1) for the DCA (samples 1 and 5) and FA (samples 1 to 5). The five samples per patient for gene expression (GE) were used to assess the temporal responses from ~1000 coding and non-coding RNAs using the nCounter system.

Results
Whole body and partial body (PB) dicentric doses, calculated using standard methods (1), were compared to the dose to blood derived using two newly developed ICR/RM dosimetric models. Initial comparisons indicate the relationship looks very promising, with a correlation of 0.860 ($p=0.001$). Success of these models will allow further development to take place. A new Bayesian method (2) was applied to the dicentric data to estimate PB doses assuming 2, 3, 4, 5 and 6 irradiated fractions. Initial results of the Bayesian analysis suggest a PB irradiation with 2 irradiated fractions is the best fit for the data in all patients. The Bayesian PB dose estimates will be compared to those calculated by the standard method and the ICR/RM models. Initial FA and GE data will also be presented.

Conclusion
To date, these initial results for conventional biomarkers indicate they can be used to validate future gene expression data. The RTGene partners will explore the possibility of combining the cytogenetic, DNA damage and gene expression data to form a multi-assay panel of biomarkers to inform on individual radiation exposure and effects. A lot more work is needed, but the next step will be validation in a larger cohort.

References
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2. Higueras et al. A new Bayesian model applied to cytogenetic partial body irradiation estimation. Radiat. Prot. Dosim. 168(3), 330-336 (2016)