RAD51 foci as biomarkers for HR efficiency and radiosensitivity in individuals with a BRCA1 or BRCA2 mutation

Stephanie Vermeulen[1,2], Valerie De Mey[1], Evi Duthoo[1,2], Anne Vral[1,2], Ans Baeyens[1,2]

[1] *Ghent University, Department of Human Structure and Repair, Radiobiology group, Ghent, Belgium*
[2] *Cancer Research Institute Ghent, Ghent, Belgium*

Background:

Breast cancer is the most common cancer in females. Known breast cancer predisposition genes are *BRCA1* and *BRCA2*. These genes are involved in the DNA damage response pathway, more specifically in homologous recombination (HR). HR is a DNA double strand break repair pathway active in S- and G2-phase of the cell cycle. Accumulation of RAD51 at the double strand break site is a hallmark of HR and could therefore be used to assess HR functionality and radiosensitivity in mutation carriers.
A recent study performed by our group showed that *in vitro* irradiation of MCF10A breast epithelial cells with reduced BRCA1 and BRCA2 protein levels resulted in a significant decrease in RAD51 foci.

Aim:
Investigate if RAD51 foci can be used as biomarkers to assess HR functionality in peripheral blood mononuclear cells (PBMCs) of healthy and *BRCA1*/*BRCA2* mutation carriers.

Methods:
PBMCs were isolated by density gradient centrifugation and cultured for 72h. The cells were irradiated with 5 Gy (220 kV X-rays). Identification of cells in S-phase at time of irradiation was achieved by EdU pulse-labelling. Thereafter RAD51 foci were detected by immunofluorescent staining and automatically scored by Metacyte software (Metafer 4, Metasystems).

Conclusion
The functional RAD51 foci assay was optimized. Preliminary results comparing RAD51 foci between healthy individuals and mutation carriers will be presented. As *BRCA1*/*BRCA2* mutation carriers might show increased risk for radiation-induced carcinogenesis, these results can ultimately contribute to personalized radiation regimens, both therapeutic as diagnostic.