Impact of radiotherapy on PBMCs DNA repair capacity: use of a functional repair assay on support

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Radiation therapy is an essential part of cancer treatment as about 50% of patients will receive radiations at least once. Significant broad variation in radiosensitivity has been demonstrated in patients. About 5-10% of patients develop acute toxicity after radiotherapy. Therefore there is a need for the identification of markers able to predict the occurrence of adverse effects and thus adapt the radiotherapy regimen for radiosensitive patients. As a first step toward this goal, and considering the DNA repair defects associated with hypersensitivity radiation syndromes, we investigated the DNA repair phenotype of patients receiving radiotherapy. More precisely, we used a functional repair assay on support to follow the evolution of the glycosylases/AP endonuclease activities of PBMCs extracts of a series of patients during the time course of radiotherapy.

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In conclusion, our preliminary results provided evidence that the DNA repair phenotype was impacted by the radiotherapy regimen. Clustering analyses of the results demonstrated a great heterogeneity of responses among the patients. Interestingly, this heterogeneity decreased between S1 and S4 with an atypical profile was also identified (p10) with increasing number of irradiations. At the end of the regimen, only 2 classes of patients remained if we except one patient that exhibited an atypical DNA repair phenotype. Furthermore, we showed that repair of several oxidized bases significantly increased between S1 and S3 or S4 (8oxoG, thymine glycol, A paired with 8oxoG), suggesting an adaptation of patients repair systems to the oxidative stress generated by the ionising radiations.

In conclusion, our preliminary results provided evidence that the DNA repair phenotype was impacted by the radiotherapy regimen. Further characterization of patients with known repair defects are needed to determine if atypical repair phenotypes could be associated with radiotherapy complications. Finally, correlation with clinical data would be useful to identify the parameters responsible for the stratification of patients in two sub-classes.

Acknowledgements: This study was funded by the CEA Program « Technologies for Health ». We thank Pr J. Balosso and Dr M. Rashkia for their involvement in patients recruitment.