Anti-cancer modalities with synchrotron radiation: a comprehensive overview considering the national context and the available data

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To date, the accidents of radiation over-dosage that recently occurred during radiotherapy treatments in Epinal and Toulouse (France) has strengthened again the absolute necessity to both evaluate the risk for over-acute reactions post-treatment and take into account the individual susceptibility to treatment. Hence, more than ever, the notion that any anti-cancer strategies should preferentially spare the normal tissues and provide with precision the corresponding *biological rather than the physical* dose, must precede any desire of increasing the dose inside tumours. In other words, the transfer of human clinical trials must be secured by a better understanding of the molecular, cellular and tissue responses to the treatment, and be based on *experimental rather than theoretical* data, obtained from replicated experiments performed in conditions as close as possible to the clinical reality (i.e. radiation dose, drug concentration and human biological material). Such requirements are inasmuch strong as the use of drugs involving in novel anti-cancer treatments is regulated and their toxicity is known through *in vitro* and *in vivo* experiments. Such requirements do concern also phase I human trials since solid experimental bases contribute to alleviate any potential law problem in case of undesired and unexpected tissue reactions. In addition to this particular national context, the development of novel anti-cancer modalities, notably targeting brain tumours, must take into account the recent advances made by the use of temozolomide, a novel alkylating agent against gliomas, and the progresses of hadrontherapy.

Hence, this is only by considering such scientific and national contexts that an overview of the considerable amount of data accumulating in the field of the anti-cancer strategies involving synchrotron radiation will be realistic and permit to go further in the development of human clinical trials. However, to reach such requirements, a number of practical constraints must be overcame: despite the enormous efforts of engineers, experiments with synchrotron radiation remain heavy to be set up and the beamtimes do not systematically permit investigators to replicate experiments in short periods to reproduce data and optimize each modality. In addition, a stand back of less than 5 years (temozolomide development began in 2000) and the variety of experimental protocols do not help in drawing solid conclusions about the *absolute* efficiency of a given anti-cancer application of synchrotron radiation.

By contrast, a rigorous quantitative analysis based on *relative* intercomparisons is already possible today and several conclusions can be drawn[1]: 1) for any anti-cancer strategy involving synchrotron, there is a quantitative correlation between rat survival and repair of DNA damage created in mimicking *in vitro* conditions; 2) modalities with iodine elicit the lowest rat survivals while those involving platinated drugs elicit the highest ones; 3) to increase the concentration of photoactivable drugs inside tumour do not lead necessarily to the increase of rat survivals; 4) while the microbeam therapy may provide similar rat survivals to modalities with platinated drugs, it has not been tested yet on human materials in order to consolidate its theoretical bases and evaluate potential overacute tissue reactions; 5) since evaluation of anti-glioma strategies is to date considerably influenced by the successful treatments with temozolomide and emerging hadrontherapy, data from

treatments already applied must be compared with those from the anti-cancer strategies involving synchrotron radiation. All these different features will be presented and discussed.

References

[1] Bencokova,Z., Balosso, J., and Foray, N. Radiobiological features of the anti-cancer strategies involving synchrotron X-rays.J Synchrotron Radiat. 2008 Jan;15:74-85.