How chemo-radiotherapy may be modeled with simple statistical mechanics rules?

J. Carlos Antoranz,[1] Mª Mar Desco,[1] and Daniel Rodríguez-Pérez[1]

[1]*Dept. Fisica Matematica y de Fluidos, UNED. Senda del Rey 9, 28040 Madrid, SPAIN*

Radiotherapy has been described numerically using different approaches to the effect of radiation on the survival of the malign tissue to be removed. The linear model, first, the linear quadratic model, later, multi-target models, with different corrections to take into account from multiple hits on the DNA, to cell interactions in the tumor, all of them have been proposed based on more or less mechanistic grounds to enhance prediction (or, at least, fit the experimental data).

Some years ago, our group introduced for this complex situation a model inspired by the complex systems thermodynamic theory: A Tsallis' entropy model. This model not only fitted well the available experimental data, or improved usual model predictions at higher dose regimes, but also raised two conjectures: the existence of a critical dose of tissue annihilation (a mathematical requirement!), and the existence of tissue-radiation specific critical exponents (as it had been shown through experimental data analysis). The mathematical structure of the model was later extended to multifractionated radiotherapy, with the only requirement of keeping the dose composition law (simple and) associative. Afterward, the continuous limit, corresponding to brachytherapy, was found to be in accordance with the non-extensive or "deformed" calculus.

These statistical mechanical results have been recently related with a cellular target-like model in which damage probability is inversely proportional to the number of healthy targets, being the proportionality constant related with the tissue-radiation exponent, and the critical annihilation dose related with the total number of targets (as could be expected). This discretization of the model leads exactly to the statistical mechanics result in the limit of infinitely many targets.

On the other hand, statistical fluctuations in the "cell population" start to play an interesting role when a finite number of targets exists: they cause some high dose effects that prevent an increased efficiency of radiotherapy as found in some types of tumors (as prostate cancer). It is remarkable that this effect does not require further assumptions as needed in other previous models of this effect. The finite-target discrete non-extensive model has also been proposed to describe the interactions between chemo- and radiotherapy, once again keeping the same simple rules derived above, and assuming that some chemopharm agents (such as cisplatin or gemcitabine) do damage the same type of cellular targets (although not exactly the same) as radiotherapy thus acting as chemosensitizers that decrease the critical annihilation dose.

These oversimplified models of radio- and chemo-radiotherapy show how non-extensivity and statistical effects may conspire to produce the wealth of behaviors described in the literature, just using a simple and small set of rules. The model might not be (radio-bio-) physically correct (it is hard to believe it is even a coarse approximation), but all we have learned from it might still be useful.