

A radiobiological database produced by the BIANCA model to predict the biological effectiveness of hadrontherapy beams

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The BIANCA (Biophysical ANalysis of Cell death and chromosome Aberrations) biophysical model [1,2] was extended and systematically applied to a wide range of particle types and energies used in cancer hadrontherapy, and the simulation outcomes were analyzed and shaped in a form suitable for an interface with a radiation transport code like FLUKA. This allowed obtaining a tool capable of predicting cell death (and possibly chromosome damage) along hadrontherapy dose profiles.

The BIANCA model, which is implemented as a Monte-Carlo code and assumes a pivotal role for DNA cluster damage, is based on the following assumptions: i) ionizing radiation can induce DNA “Cluster Lesions”(CLs), where a CL is defined as a critical DNA damage that produces two independent chromosome fragments; ii) chromosome fragment un-rejoining, or distance-dependent mis-rejoining, gives rise to chromosome aberrations; iii) certain aberrations (dicentric, rings and large deletions) lead to cell death. The yield of CLs is the first adjustable parameter, and its value is tuned for each radiation quality following comparison with experimental data taken from the literature; in the model version applied in this work, the second, and last, model parameter is the chromosome-fragment unrejoining probability.

The simulation outcomes were systematically tested against experimental data on cell lines of different radiosensitivity exposed to different particles over a wide energy range. Good agreement was obtained, which allowed producing a database of CL yields for different particle types and LET (Linear Energy Transfer) values. Before the so-called “overkilling region”(the high-LET region where the biological effectiveness stops increasing), for each ion type the CL yield showed a LET-dependence of the form $a \cdot L + b \cdot L^2$, thus allowing to establish a one-to-one correspondence between LET value and CL yield; in the overkilling region, a tendency to saturation was observed and other functions were tested. Thanks to these fits, the CL input parameter can now be derived a priori for every LET value, including those not investigated experimentally.

It was therefore possible to perform many simulations of cell survival for protons, He- and C-ions over a wide LET range (at steps of few keV/ μm) and for several doses, using as input the CL yields provided by the fits. Each simulated survival curve was then fitted by a linear-quadratic exponential function of the form $S(D) = \exp(-\alpha D - \beta D^2)$. This allowed to produce an almost continuous set of α and β values as a function of LET for each ion type.

In the context of hadrontherapy, the tables of α and β values provided by BIANCA can be read by FLUKA, which provides all the necessary information (particle type, LET and absorbed dose), thus allowing fast computing of biological outputs in every position of a therapeutic dose profile.

1. M.P. Carante and F. Ballarini (2016), Calculating Variations in Biological Effectiveness for a 62 MeV Proton Beam. *Front. Oncol.* 6:76.
2. F. Ballarini and M.P. Carante (2016), Chromosome aberrations and cell death by ionizing radiation: evolution of a biophysical model. *Radiat. Phys. Chem.* 128C, 18-25.

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Primary authors: CARANTE, Mario Pietro (INFN - National Institute for Nuclear Physics); TELLO CAJIAO, John James (Universidade Estadual de Campinas.); BALLARINI, Francesca (University of Pavia and INFN - National Institute for Nuclear Physics)

Presenter: CARANTE, Mario Pietro (INFN - National Institute for Nuclear Physics)

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