Modeling time effects in the incidence of deterministic effects of radiation

L. Herr[*1,2], *T. Friedrich*[1,2], *M. Durante*[1,2], *and M. Scholz*[1]
[1]GSI, Darmstadt, Germany; [2]TU Darmstadt, Germany

The Giant LOop Binary LEsion (GLOBLE) model is applicable to model time effects in the cellular response to photon radiation. Since the incidence probability for deterministic effects after irradiation, e.g. pneumonitis or the bone marrow syndrome, is thought to be closely linked to cell death, it was tested whether one can qualitatively reproduce time effects in this incidence probability with the GLOBLE model. It was found that with a decrease of the dose rate during exposure, the GLOBLE model describes very well the clinically observed increase of the dose where 50% of the patients are expected to suffer from a disease.

Methods

The GLOBLE model

The setup of the GLOBLE model is presented in detail in [1]. Briefly, the cellular response to photon radiation is predicted based on two classes of DNA double strand breaks. Isolated DSB (iDSB) reflect single DSB in DNA giant loops and are extpected to be quickly repaired by a cell (half-life time HLT_i) with low lethality (ϵ_i). Clustered DSB (cDSB) represent two or more DSB in a loop and go in hand with a long half-life time (HLT_c) and a high lethality (ϵ_c). Since the total number of DSB is assumed to be constant for a given dose, initially induced DSB are temporarily separated when the dose is protracted over a longer time. Consequently, single DSB in a giant loop might be repaired by a cell before a next DSB occurs in the same loop and the fraction of harmful cDSB decreases. The extent of the inherent reduction of the effectiveness of radiation depends crucially on the rates of DSB induction and repair and can be calculated with the GLOBLE model.

Deterministic effects of radiation

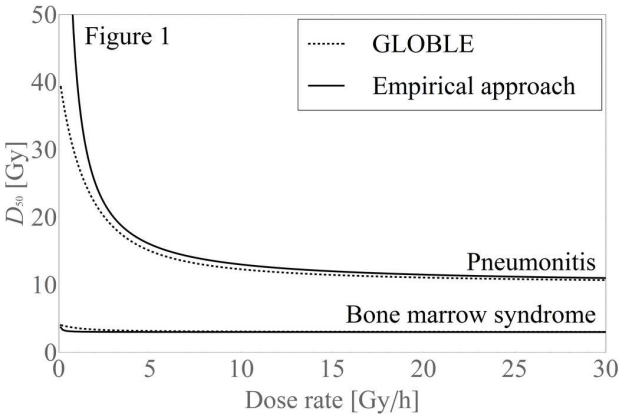
Clinically, it has been observed that the dose D_{50} at which 50% of the exposed patients start to show symptoms attributed to deterministic radiation effects depends linearly on the inverse of the applied dose rate $\dot{D}$ [2]:

$$D_{50}(\dot{D}) = \theta_\infty + \frac{\theta_1}{\dot{D}} \qquad (1)$$

For pneumonitis and the bone marrow syndrome it has been found that D_{50} after acute exposure is θ_∞ = 10 Gy and θ_∞ = 3 Gy, respectively. The extent of the dose rate effect is represented by θ_1 = 30 Gy^2/h and θ_1 = 0.07 Gy^2/h, respectively. The solid lines in figure 1 represent the graphs corrsponding to this empirical approach.

In order to describe time effects in the incidence of deterministic effects with the GLOBLE, pneumonitis and bone marrow syndrome specific parameters found in literature were converted to ϵ_i = 0.00333, ϵ_c = 0.229 and ϵ_i = 0.00333, ϵ_c = 0.09, respectively. In agreement with experimental observations about DSB repair, HLT_i was set to 0.5 h and HLT_c to 5 h.

Results



The dashed graphs in figure 1 represent the GLOBLE predictions for time effects in the incidence of deterministic effects after radiation exposure. Obviously, there is a very good agreement with empirical observations (solid lines) down to dose rates of $\dot{D} \approx 3$ Gy/h. A large increase of D_{50} with decreasing $\dot{D}$ is expected for pneumonitis whereas the increase in D_{50} is small for the bone marrow syndrome. Deviations between the empirical formulation (1) and the GLOBLE model at lower dose rates are due to the empirical prediction of infinite D_{50} for $\dot{D} \to 0$. Since finite D_{50} at low $\dot{D}$ are more plausible, the GLOBLE might provide an advantage in the assessment of the incidence probability of deterministic radiation effects at low dose rates. The general good perfomance of the GLOBLE model demonstrated here supports its potential to be clinically applied.

References

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* l.herr@gsi.de, supported by Studienstiftung des deutschen Volkes and HGS-Hire.