Radiobiological modeling in radiation oncology

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Abstract
Radiobiological models are widely used to predict the outcome of radiation therapy based on dose distribution characteristics. The need for these models has emerged as radiotherapy practice has evolved. In the past, the optimization process in radiotherapy was performed through trial and error by calculating and comparing multiple treatment plans. While, to this end with new technologies in radiotherapy manual optimization is no longer practical and automated optimization algorithms have been developed. Most of these algorithms use absorbed dose in an objective function used in the planning process. However, dose is clearly a surrogate for biological response. This study provides an overview of the present status of radiobiological models that can be used for treatment planning in radiation therapy.
Keywords: Radiobiology, radiobiological modeling, radiotherapy, TCP, NTCP

Recently radiobiological models in terms of mathematical models are widely used to predict the outcome of radiation therapy based on dose distribution characteristics (1,2). The need for these models has emerged as radiotherapy practice has evolved. In the past, the process of optimization of radiation treatment was preformed through trial and error by calculating and comparing multiple treatment plans and has consisted of maximizing the dose to the tumor while at the same time minimizing the dose to normal tissues (3,4). Recently, with new technologies, and specifically the use of intensity-modulated radiation therapy (IMRT), a tremendous control over a very precise and conformal dose delivery in three dimensions is allowed. In other words, manual optimization is no longer practical (5-7).

To this end, automated optimization algorithms based on the radiobiological models have been developed. The ultimate goal of these algorithms in radiation therapy is to generate uncomplicated cures, i.e., maximizing tumor control probability (TCP) while at the same time minimizing the normal tissue complication probability (NTCP) (8, 9). Ideally, in the planning process optimization algorithms should use objective functions that incorporate mathematical models accounting for the various parameters associated with radiobiological response in radiation treatment, such as total dose, dose per fraction, overall treatment time, time between fractions, dose rate, volume irradiated, and, possibly, modifying agents such as radiation sensitizers or chemotherapy (10-12).

Many of the factors just listed involve the use of fractionation in radiation therapy. The basis of fractionation effects in radiation therapy has been well studied both in the laboratory and in the clinic, although it is recognized that adequate clinical data are still lacking to allow for a thorough analysis of radiobiological models. Classic textbooks describing fractionation effects appeal to the four “R’s” of radiobiology: 1) repair of sublethal damage, 2) reassortment of cells within the cell cycle, 3) repopulation, and 4) reoxygenation. Fractionation helps spare normal tissues through repair and repopulation and increases tumor cell kill due to re-assortment and re-oxygenation. In addition, overall time affects response. Prolongation of treatment time results in sparing of early reactions and allows re-oxygenation in tumors, although excessive prolongation will allow tumor cells to proliferate (10-12).

Radiobiological models can generally be divided into two broad classifications: empirical models and mechanistic models. Empirical models are based on mathematical expressions that have been fit to experimental data, but no real account is taken of the underlying mechanisms associated with the response. Mechanistic models aim to incorporate some of the underlying radiobiological response mechanisms (12-14). However, because of the complicated nature of biological response to irradiation, the reality is that most of the existing radiobiological models are largely empirical. In these models, the quality of data fitting and the utility of prediction are dependent on the mathematical expressions used and how closely they emulate some of the components of the response mechanisms.

The most commonly used model today is the linear-
Implication for health policy/practice/research/medical education

Recently, radiobiological models are widely used to predict the outcome of radiation therapy based on dose distribution characteristics. The need for these models has emerged as radiotherapy practice has evolved. To this end, for modern radiotherapy automated optimization algorithms have been developed. Most of these algorithms use absorbed dose in an objective function used in the planning process. However, dose is clearly a surrogate for biological response, since the goal of radiation therapy is to generate uncomplicated cures, i.e., maximizing tumor control probability (TCP) while at the same time minimizing the normal tissue complication probability (NTCP).

quadratic (LQ) model, which uses a mathematical formulation that relates to cell survival; certain factors affecting survival, such as repair and proliferation, can be readily incorporated (12).

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References