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Review

Ion-beam cancer therapy: News about a multiscale approach to radiation damage

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ABSTRACT

We report the present stage of development of our multiscale approach to the physics related to radiation damage caused by irradiation of a tissue with energetic ions. This approach is designed to quantify the most important physical, chemical, and biological phenomena taking place during and following such an irradiation in order to understand the scenario of the events leading to cell death and provide a better means for clinically necessary calculations with an adequate accuracy. On this stage, we overview the latest progress in calculating energy spectra of secondary electrons in liquid water and the results of an application of the inelastic thermal spike model to liquid water in order to calculate the heat transfer in the vicinity of the incident-ion track. The dependence of energy distributions of secondary electrons, resulting from ionization of the liquid water, on the energy of primary ions is studied in two regimes. For slow ions, a new parameterization of energy spectra in liquid water is suggested. For fast ions, different dispersion schemes on the basis of a dielectric response function approach are used and compared. Thermal spike calculations indicate a very large temperature increase in the vicinity of ion tracks near the Bragg peak during the time interval from 10^{-15} to 10^{-9} s after the ion's passage. An increase of pressure, as large as tens of MPa, can also be induced during that time. These effects suggest a possibility of thermo-mechanical pathways to disruption of irradiated DNA. A combination of a temperature spike and electron/hole interactions may be a dominant pathway of DNA damage.

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1. Introduction

For more than 10 years, heavy-ion-beam cancer therapy has been successfully used clinically in Germany and Japan. Proton-beam therapy is performed in many more centers around the globe and even more are under construction. Thousands of patients per year are being treated. These therapies appear to be a more favorable alternative to the conventional photon therapy [1–3].

The new therapies have several advantages compared to the photon therapy. These advantages can be quantified using the so-called Relative Biological Effectiveness (RBE). The RBE is a ratio of the dose (energy deposited to the tissue) due to photons to that due

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to the projectiles used in a given therapy bringing about the same biological effect. The larger is this ratio in particular conditions (location of a tumor, presence or absence of oxygen on site, etc.) the better is the therapy suited; e.g., protons may be better than heavier ions for some parts of the tumor and vice versa. Apparently, the RBE is the most significant value for making a decision about the desired therapy. At the same time, in the process of calculation of the RBE, the minimal required dose can be determined as well as other instructions to the radiologists designing treatment.

The problem is, however, that the RBE, cannot be easily calculated. At the moment, it is either determined empirically (with many limitations) or theoretically (e.g., based on the Local Effect Model [4,5]). A phenomenon-based (if not an *ab initio*) calculation of the RBE is very much desired; however, the scenario of events from the incidence of an ion onto tissue to the cell death is not quantified. Moreover, some important processes are not understood even on a qualitative level. The main obstacle to understanding radiation damage to DNA (deemed to be mostly responsible for cell death [6–9]) is that microscopic events happen on many spatial, temporal, and energetic scales; e.g., time scales for relevant processes vary from 10^{-22} s to minutes, hours, or even longer times. Indeed, 10^{-22} s is the characteristic time of nuclear reactions, which take place when an incident ion collides with nuclei of the medium; 10^{-15} s is that of ionization and excitation of molecules of the medium, which are the leading processes of energy loss by the projectile, 10^{-12} s is that of transport of secondary electrons formed as a result of the above ionization, 10^{-5} s is that of DNA damage, and longer times correspond to DNA repair by different mechanisms.

The claim of our multiscale approach to the physics of ion-beam cancer therapy is that the phenomenon-based calculation of the RBE is possible if we evaluate the most important physical, chemical, and biological effects that happen in the process of irradiation and (mainly biological) processes following irradiation on longer time scales. Instead of reconstructing the sequence of events using scale-dependent Monte Carlo (MC) simulations, we consider phenomena on all scales and combine them in a complete picture [10–16].

The understanding of the scenario of radiation DNA damage and repair is an interdisciplinary science problem, and its whole scope is shown in Fig. 1.

From this figure, one can see that this problem joins different areas of physics, different areas of chemistry, and different areas of biology. This scope is too vast for being taken on all scales simultaneously and in the beginning we limited our considerations to physical and some chemical phenomena. At this moment our multiscale approach consists of analyses of ion propagation in a medium, production and transport of secondary electrons, and different pathways of DNA damage and their quantification.

A good complement to this analysis, also focused on the peculiarity of the medium, is a research in liquid water femtochemistry [17], which explores the consequent damage done by radicals after the physical stage that we describe in this paper.

2. Ion propagation in tissue and energy spectra of secondary electrons

The first advantage of hadron-beam therapies, most obvious to physicists, is related to the fashion in which charged massive projectiles lose energy in the process of deceleration in tissue, because macroscopically, all therapeutic effects are due to this

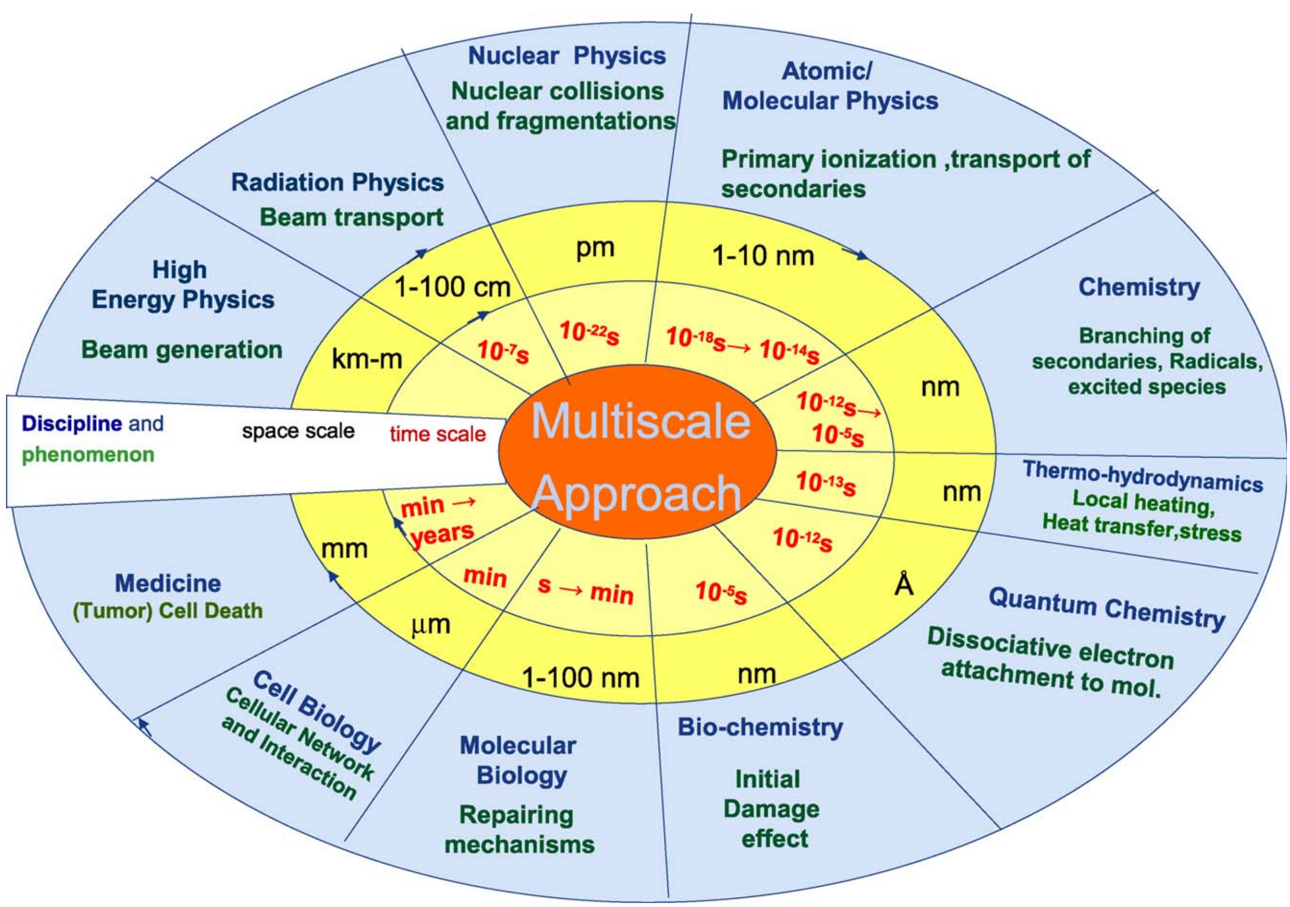

Fig. 1. The scientific palette of phenomena involved in ion-beam cancer therapy.