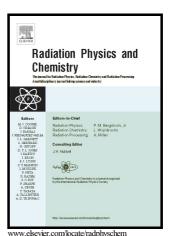
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ACCEPTED MANUSCRIPT

Actual questions raised by nanoparticle radiosensitization

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Abstract

Radiosensitization by metallic nanoparticles (NP) has been explored for more than a decade with promising results *in vitro* and *in cellulo* reported in a vast number of publications. Yet, few clinical trials are on-going. This could be related to the lack of selectivity of NP leading to massive quantities to be injected to observe an effect but also to the higher degree of complexity than first thought leading to an absence of consensus probably caused by the lack of standardization in pre-clinical studies. Given the wide panel of NP used, in terms of core nature, size, coating, not to mention of cell lines and irradiation modalities, cross-comparison of data is not a walk in the park. But only a thorough examination could help identifying the key parameters and the possible mechanisms involved. This step is crucial as it should provide guidance for designing the most efficient combination NP/radiation and rationally establishing clinical protocols. In this review, we will combine and confront cellular radiosensitization results with *in vitro* and numerical experiments in order to give the more recent vision of this complex phenomenon. We decided to address a few hot topics such as the influence of the incident radiation energy, the localization of NP or the so-called "biological" effect. We will highlight that among the barriers to break down, some are not restricted to the "nano" community: an incontestable support could be offered by the "radiation" community in the broadest sense.

Keywords. nanoparticles, radiotherapy, radiosensitization, radiobiology

Introduction

Nanotechnology appears to be a very attractive field as huge amount of public and private funds are now devoted to this area. For example, Google Inc. recently patented several sensor devices based on an increased sensitivity due to nanoparticles (NP). As regards public funding, through the Seventh Research and Innovation Funding Program (FP7), the European Commission invested nearly 3.5 billion euros for 2007–2013 in the "Nanosciences, Nanotechnologies, Materials and New Production Technologies" project. As for Horizon 2020, which is the European Union's largest ever research endeavor (80 billion euros over 7 years), it explicitly aims to bridge the gap between nanotechnology research and markets, especially in health domain. Effective translation of nanotechnologies for medical applications is said to concern three main areas: therapeutics,

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