Relative Biological Effectiveness of Neutrons for Cancer Induction and Other Late Effects: A Review of Radiobiological Data

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Abstract

The risk of secondary cancer induction after a therapeutic irradiation with conventional photon beams is well recognised and documented. However, in general, it is totally overwhelmed by the benefit of the treatment. The same is true to a large extent for the combinations of radiation and drug therapy. After fast neutron therapy, the risk of secondary cancer induction is greater than after photon therapy. This can be expected from the whole set of radiobiological data, accumulated so far, which shows systematically a greater relative biological effectiveness (RBE) for neutrons for all the biological systems which have been investigated. Furthermore, the neutron RBE increases with decreasing dose and there is extensive evidence that neutron RBE is greater for cancer induction and for other late effects relevant in radiation protection than for cell killing at high doses as used in therapy. Almost no reliable human epidemiological data are available so far, and the aim of this work is to derive the best risks estimate for cancer induction after neutron irradiation and in particular fast neutron therapy. Animal data on RBE for tumour induction are analysed. In addition, other biological effects are reviewed, such as life shortening, malignant cell transformation in vitro, chromosome aberrations, genetic effects. These effects can be related, directly or indirectly, to cancer induction to the extent that they express a "genomic" lesion. Since neutron RBE depends on the energy spectrum, the radiation quality has to be carefully specified. Therefore, the microdosimetric spectra are reported each time they are available. Lastly, since heavy-ion beam therapy is being developed at several centres worldwide, the available data on RBE at low doses are reviewed. It can be concluded from this review that the risk of induction of a secondary cancer after fast neutron therapy should not be greater than 10–20 times the risk after photon beam therapy. For heavy ions, and in particular for carbon ions, the risk estimate should be divided by a factor of about 3 due to the reduced integral dose. The risk has to be balanced against the expected improvement in cure rate when the indication for high-LET therapy has been correctly evaluated in well-selected patient groups.
Introduction

Accurate knowledge of the neutron relative biological effectiveness (RBE) for cancer induction is of paramount importance in radiation protection for assessing the risk related to a neutron exposure and for setting appropriate dose limits.

In radiation therapy also, it is essential to know, as accurately as possible, the neutron RBE for late effects and in particular for cancer induction.

Induction of a secondary cancer by a radiological and/or medical treatment has always been a great source of concern for the radiation oncologist as well as for the medical oncologist. Radiation-induced cancers have indeed been reported after radiation treatment by many authors, in particular for locally extended cervix carcinomas (Day and Boice 1983; Boice et al. 1988), and also after a combination of radiation and drug therapy (de Vathaire et al. 1989; Tucker et al. 1988; Curtis et al. 1992). However, in most cases, the benefit of the treatment (in terms of survival, local control and quality of life) largely overwhelms the risk of secondary cancer induction after photon irradiation. As an example, Fig. 1 and Table 1, taken from an International Agency for Research on Cancer (IARC) study, give the risk of cancer associated with a broad range of organ doses, after radiation therapy for cervical cancer. A total number of 150 000 patients with cervical cancer were followed, and 4188 secondary cancers were observed. Table 2 illustrates the increased risk after combination of radiation therapy and chemotherapy.

The risk of secondary cancer induction, after fast neutron therapy, is greater than after conventional photon therapy, as can be anticipated from the available radiobiological data indicating high RBE values for cancer induction after neutron irradiation. However, as in photon therapy, for well-selected groups of patients, the benefit due to the treatment with high linear energy transfer (LET) radiations is definitely higher than the increased risk of secondary cancer induction. It is one of the reasons why the clinical indications for high-LET radiation therapy need to be well evaluated; this problem is discussed at length in the different chapters of the present book.

As a generally practised approach, high-LET radiations should not be applied to children because of the increased risk of secondary cancer induction. This is important to consider if long survival is expected (Wamborsie et al. 1982).

In conventional photon therapy, patients are also exposed to low doses of neutrons when the beam energy exceeds about 10 MV (Karzmark 1987; Karzmark et al. 1993).

The production of neutrons from high-energy medical accelerators has been evaluated by Nath et al. (1984). Firstly, neutrons are produced by high-energy photons incident on the various materials of the target, flattening filter, collimation system and other essential components of the machine. For a given photon observed dose to the target volume, the neutron yield increases rapidly with the energy of the photons from 10 to 20 MV, but remains rather