A Study on Differences between Radiation-induced Micronuclei and Apoptosis of Lymphocytes in Breast Cancer Patients after Radiotherapy

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Cancer patients’ responses to radiotherapy vary in severity. It has been suggested that it may be due to differences in intrinsic cellular radiosensitivity. Prediction of tissue reactions to radiotherapy would permit tailoring of dosage to each patient. Towards this goal the micronucleus and apoptosis tests have been proposed as methods for measurement of chromosomal damage in peripheral blood lymphocytes. In this study, gamma-ray sensitivity of cultured lymphocytes of 26 breast cancer patients with early or late reactions was investigated. After irradiation with 4 Gy gamma radiation in $G_0$, the frequency of micronuclei for patients with early reactions was significantly higher ($P < 0.05$) than for patients with late reactions. In the contrary the frequency of apoptosis for patients with early reactions was significantly lower ($P < 0.05$) than in the other group. It could be suggested that such a reduced amount of micronuclei in the late effects group is due to the presence of some residual DNA damages which are not completely repaired and lesions show increasing severity when the patients’ cells are irradiated again. These induced damages, probably are high enough to stimulate other endpoints like apoptosis instead of micronuclei.

Key words: Breast Cancer, DNA Damage, Radiosensitivity

Introduction

Cancer patients’ responses to radiotherapy vary in severity (Tucker et al., 1992; Turesson et al., 1996). A range of normal tissue reactions is seen in patients, from very mild to extremely severe and occasionally lethal (Turesson and Thames, 1989). A major determinant of normal tissue reaction is the intrinsic radiosensitivity of the cells (Turesson, 1990).

Much of radiobiology is concerned with increasing our understanding of why and how normal tissues and tumors respond to radiation with the ultimate aim of improving cancer treatment by radiotherapy. Hence the need for reliable predictive assays for normal tissues and tumors response to radiation remains a prime objective of clinical oncology.

The micronuclei assay and apoptotic cell death are biological indicators for assessment of radiosensitivity (Muller et al., 1996; Hendry and West, 1997).

The complexity and laboriousness of enumerating aberrations in metaphases has stimulated the development of a simpler system of measuring chromosome damage. Schmid and Heddle proposed independently that measuring micronuclei is an alternative and simpler approach to assess chromosome damage in vivo (Schmid, 1975; Heddle, 1973). Micronuclei are discrete round bodies of nuclear origin found in the cytoplasm outside the main nucleus. They are expressed in dividing cells that either contain chromosome breaks lacing centromeres (acentric fragments) and/or whole chromosomes that are unable to travel to the spindle poles during mitosis. At telophase, a nuclear envelope forms around the lagging chromosomes and fragments, which then uncoil and gradually assume the morphology of an interface nucleus with the exception that they are smaller than the main nuclei in the cell, hence they are “micronuclei”. In 1985 Fenech and Morley found that the addition of cytochalasin B (cyt B) to the culture medium prevents cells from completing the division cycle by inhibiting cytokinesis but not karyokinesis. By using this technique, cells with only one mitotic division since the addition of cyt B included two nuclei (Fenech and Morley, 1985a, b).