DNA Double Strand Breaks in Mammalian Cells Exposed to γ Rays and Heavy Ions ◇

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The most commonly observed damage to cells following irradiation is the presence of base damage, single- and double-strand breaks (DSB) in the DNA. Cells react to those damages in various ways, depending on the severeness of the damage. This could be complete repair of the damaged DNA, mutation resulting from misrepair, or the death of the cell.

In the view of the growing interest in the action of ions on cells in medicine and space research the determination of the distribution of DNA fragments is an important tool to characterise the biological effects. The measurements are done using the pulsed field gel electrophoresis (PFGE) technique. It was seen that exposure to γ-rays produces distribution of DNA fragment lengths that are in accord with a uniform statistically independent distribution of DSB, i.e. the distribution of DNA fragments resulting from sparsely ionising radiation like γ-rays is predictable using a random breakage model (fig. 1).

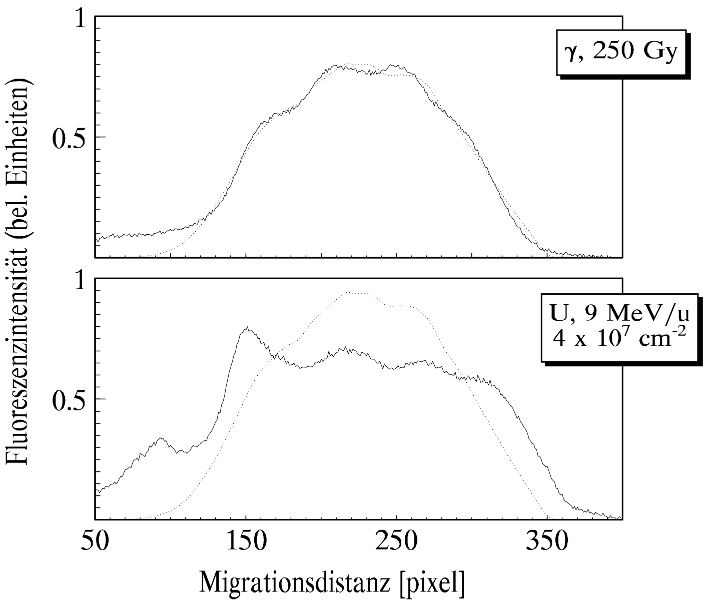

Fig. 1: Measured DNA-spectra (thick line) after irradiation of V79 cells with sparsely ionising radiation (upper diagram) and densly ionising radiation (lower diagram). The dotted line represents the best fitted calculated profiles resulting from the random breakage model [1]

Exposure to heavy ions results in substantially overdispersed distributions which indicates that the fragmentation of the DNA is not a statistically independent process. Heavy ions induce multiple damage sites on the DNA strand. These measurements were done recently using densely ionising by different authors, but there is very little data available in the intermediate LET range.

First experiments using a 25.8 MeV proton beam and a 40.5 MeV α particle beam were done at the vertical beamline of the Tandem Accelerator. The results are under evaluation. The data is obtained by irradiation of V79 cells. The DNA is extraced out of these cells and put into a pulse field gel, in order to measure the length distribution of the DNA fragments after the irradiation. A typical gel is shown in fig. 2.

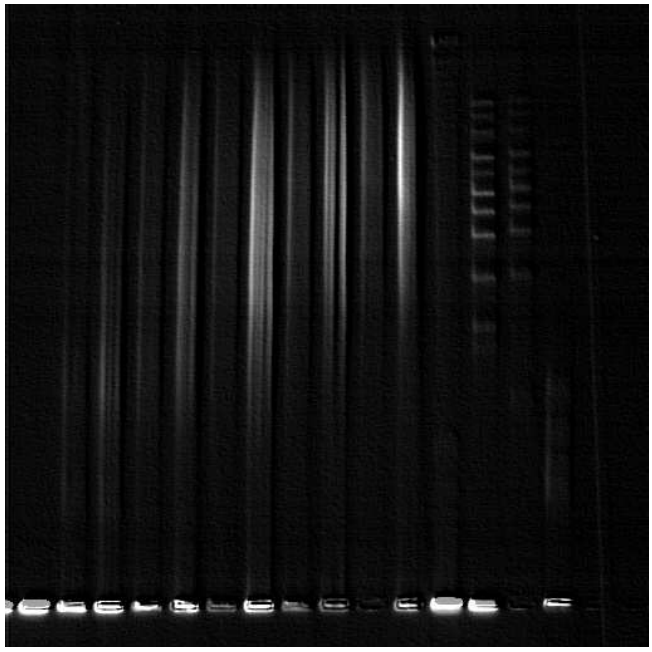

Fig. 2: Pulse field electrophoresis gel; 25.8 MeV proton vs gamma irradiated DNA

The lanes in this gel show the stained DNA irradiated with gamma radiation and 25.8 MeV protons at the vertical beamline. In addition to the irradiated DNA, a number of length standards are seen on the right hand side of the gel. The dose steps selected in this irradiation experiments are 100 Gy to 500 Gy in steps of 100 Gy.

The width of the DNA distribution for protons is wider than the width of the distribution for gamma irradiated DNA, which indicates that protons tend to induce multiple damage sites on the DNA strand.

In order to give quantitative statements further detailed investigations are planned.

References

[1] A. M. Kraxenberger, Ph.D. thesis 1995

[2] Eric J. Hall, in textiRadiobiology for the Radiologist, 4th Edition, J.B. Lippincott Company, 1994

◇ Supported by the Bavarian Minister for Environment