Investigation of X-ray and ion irradiated DNA using scanning force microscopy

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It is well known that the biological effectiveness for cell inactivation of radiation with high linear energy transfer (LET) around 100 keV/µm is higher than the one of low-LET radiation [1]. The reason for that may rely on the fact that double-strand breaks (DSB) of DNA-molecules induced by high-LET-radiation are repaired less efficiently than those, which are induced by low-LET-radiation [2]. This could be caused by a different spatial distribution of DSB, in connection with the inhomogeneous distribution of dose. To verify this hypothesis it is desirable to directly investigate the condition of DNA after irradiation.
In our work we did these investigations on plasmid DNA irradiated with X-rays and ions using scanning force microscopy (SFM). Therefore we developed a preparation method which allowed us to determine the fractions of the different plasmid conformations and additionally measure the length of DNA fragments in the pictures produced by the SFM (see Figure 1)

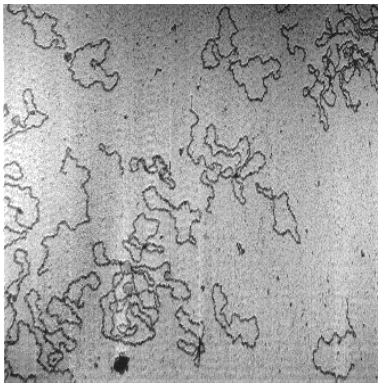

Figure 1: Typical SFM picture of DNA
(size: 3µm x 3 µm)

Using this preparation method we studied ΦX174 plasmid DNA that was irradiated in 20 mM HEPES buffer in a supercoiled compact conformation with different doses of X-rays and Zn-ions.
As a result we obtained for every sample the fraction of each different plasmid conformation (see Figure 2) and the fragment distributions. From this we were in addition able to determine the mean fragment-lengths as well as the number of DSB per broken plasmid (see Figure 3).
In figure 2 the difference between high- and low-LET radiation in the production of DNA-DSB can be seen. For X-rays the linearised fraction increases quadratically with dose while for ions in the lower dose region this fraction increases linearly.

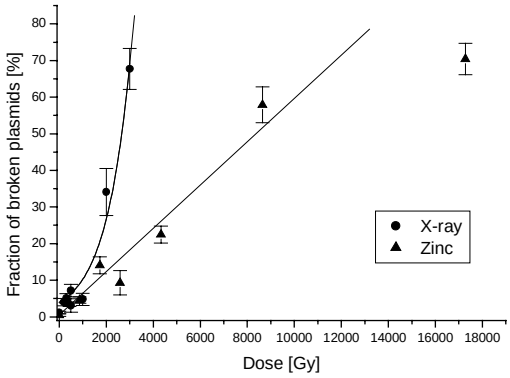

Figure 2: Fraction of broken plasmids

Figure 3 shows that the number of DSB per broken plasmid after high-LET irradiation with low doses is significantly higher than 1. After low doses of X-ray irradiation this number appears to be smaller than that after ion irradiation but it increases steeper with dose.

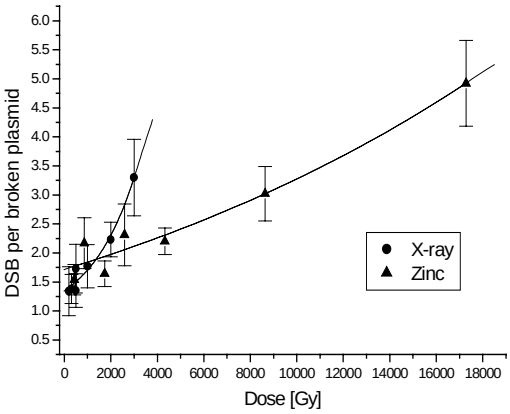

Figure 3: Number of DSB per broken plasmid

These results point to a spatial correlation of the induction of DSB's by densly ionising particles.
Yields of DSB per broken plasmid need to be further investigated at low fluences.

[1] W. K. Weyrather et al.; Int. J. Radiat. Biol. 75, 11, 1357-1364 (1999)

[2] G. Taucher-Scholz et al.; Radiat. Environ. Biophys. 34, 101-106 (1995)