DNA fragmentation induced by ionizing radiation – Atomic Force Microscopy study

and biophysical modeling.

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DNA as a carrier of genetic information is considered to be the critical target for radiation induced damage. Especially severe are DNA double-strand breaks (DSBs), formed when breaks occur in both strands of the molecule. The DSBs production is determined by the spatial distribution of ionization events, dependent on the physical properties of the energy deposition and the chemical environment of the DNA.

According to theoretical predictions, high LET charged particle radiation induces lesions in close proximity forming so called clustered damage in the DNA. Atomic Force Microscopy (AFM) was newly established as a technique allowing the direct visualization of DNA fragments resulting from DSBs induced in small DNA molecules (plasmids) by ionizing radiation.

We have used AFM to visualize the DNA fragmentation induced by heavy ions (high LET radiation) and to compare it to the fragmentation pattern obtained after X-rays (low LET radiation). Plasmid supercoiled DNA was irradiated in vitro with X-rays and 3.9 MeV/u Ni ions within a dose range 0 – 3000 Gy. Afterwards, the samples were analyzed using AFM, which allowed the detection and length measurement of individual fragments with a nanometer resolution. Recording of the length of the induced fragments allowed to distinguish between molecules broken by a single DSB or by multiple DSBs. The fragment length distributions were derived for different doses and different radiation qualities.

The first results of the measurement of radiation-induced DNA fragmentation show an influence of radiation quality on the DSB production. A theoretical approach based on the track structure which models clustered DSB formation in terms of a compound Poisson process is presented. Its predictions on formation of DNA fragments are discussed.