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# Induction of complex DNA damage after proton therapy beam irradiation to plasmid DNA and human prostate cancer cells

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## Background

DNA damage is the key to cancer RT, as they facilitate treatment optimization, leading to more precise and effective tumor targeting while minimizing damage to surrounding healthy tissues. In this study complex DNA damage was measured in **DU145 prostate cancer cells** irradiated along 62.4 MeV proton beam and **plasmid pBR322** across a **proton treatment plan** (137-198 MeV, LET 1-9 keV/μm) at MedAustron Ion Therapy Center.

## Materials & Methods

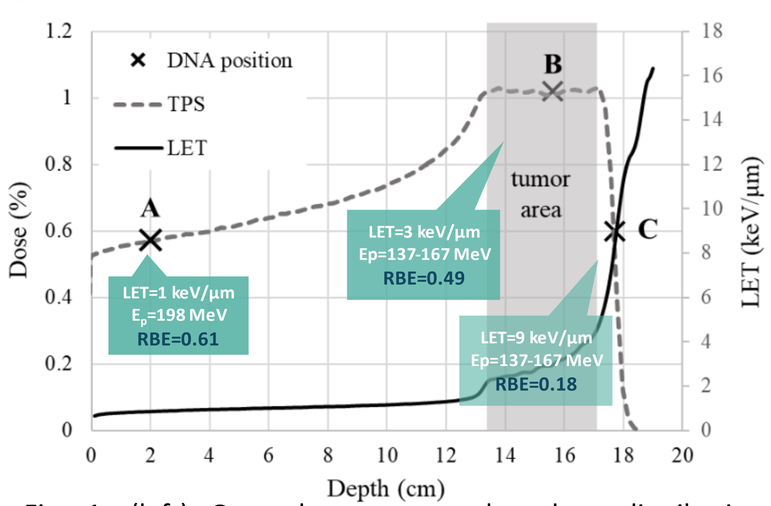
**Agarose gel electrophoresis** highlights the crucial role of LET and Reactive Oxygen Species in DNA fragmentation and **Atomic Force Microscopy** (AFM) was utilized to measure apparent plasmid lengths, providing insights into the impact of increasing LET on the induction of highly complex DNA damage. **Immunofluorescence** was employed to detect complex damage in DU145 cells.

## Results

Increased level of DNA damage complexity at the SOBP and distal SOBP fall off. Relative Biological Effectiveness (RBE) for Double strand break (DSB) induction for protons compared to X rays (control radiation) has been calculated. An apparent RBE value of 0.61 at the entrance, 0.49 in the SOBP plateau, and 0.18 at the SOBP fall-off was found. For human prostate cancer cells DU145, we detected a significant induction of complex damage at the distal SOBP fall-off, where highest LET is expected.

## Conclusion

This study highlights the limitation of constant RBE adoption and emphasizes the necessity for novel biomarkers to overcome existing limitations in complex DNA damage detection.



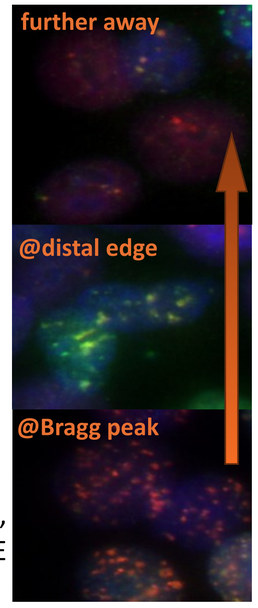
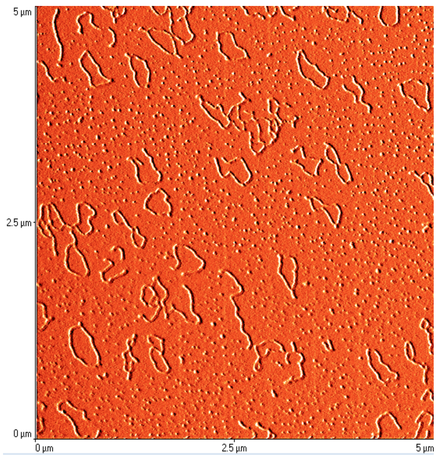




Fig. 1: (left) General treatment plan dose distribution, **plasmid pBR322** irradiation parameters and apparent RBE values along the therapeutic proton SOBP. (right) **γH2AX** & **53BP1** signal of **DU145 prostate cancer cells** along a mono-energetic proton beam of 62.4 MeV protons.



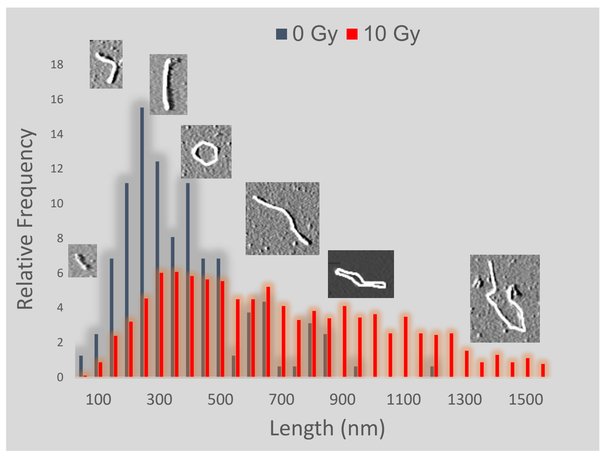



Fig. 2: A representative AFM image (5μm×5μm) of plasmid pBR322, revealing the DNA macromolecule conformations. The relative frequency distribution of apparent molecule lengths for control sample (0 Gy) and irradiated with 10 Gy (proton beams) together with AFM images of DNA molecules of different forms.