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## Enhancement of the biological effectiveness in the bragg peak: a nanodosimetric perspective

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In proton therapy, a constant relative biological effectiveness (RBE) of 1.1 is currently recommended and used in clinics. This is despite the fact that this quantity varies (for example with the depth of the proton beam) in a medium, which also causes a change in the biological beam range. Various authors have noted that it is worth considering these variations in treatment planning, especially for beams pointing towards or passing laterally adjacent to organs at risk. These variations are strongly dependent on the physical properties of the beam as well as on absorbed dose and the biological properties of the irradiated tissue.

To study the physical properties of proton tracks, we examined biological effectiveness in terms of novel nanodosimetric quantities related to track structure based on the formation of ionisation clusters in target volumes, comparable in mass per unit area, to a DNA segment. The track structure of different ionising radiations can be characterised by nanodosimetric quantities derived through measurements and numerical simulations.

In this study we present an investigation of the variation of nanodosimetric parameters with depth in the proton beam leading up to the Bragg peak region, which is an indication of the variation in biological effectiveness. Simulations are performed using the GEANT4-DNA extension toolkit that can simulate physics processes using models that can track step-by-step interactions of particles in liquid water down to the eV scale. The DNA target is modeled by a cylindrical volume of water with dimensions comparable to a DNA segment of 10 base pairs. These targets are placed at various positions in and around the track to map out the variation of nanodosimetric parameters.

The results of this investigation demonstrate an ionisation cluster size distribution that shows an enhanced biological effectiveness at track ends (Bragg peak region). The enhancement of the biological effectiveness is observed in and off track axis. This result is in contrast to the clinically accepted use of a constant RBE value of 1.1 for protons.

### Country

South Africa

### Institution

National Metrology Institute of South Africa (NMISA) & University of the Witwatersrand

**Primary author:** NGCEZU, Sonwabile (National Metrology Institute of South Africa & University of Witwatersrand)

**Co-authors:** VAN DER MERWE, Debbie (University of the Witwatersrand); RABUS, Hans (Physikalisch-Technische Bundesanstalt (PTB)); BUG, Marion (Physikalisch-Technische Bundesanstalt (PTB))

**Presenter:** NGCEZU, Sonwabile (National Metrology Institute of South Africa & University of Witwatersrand)

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