A Novel Biomolecular Dosimetry Metric for Biological Assessment of Particles and Ions

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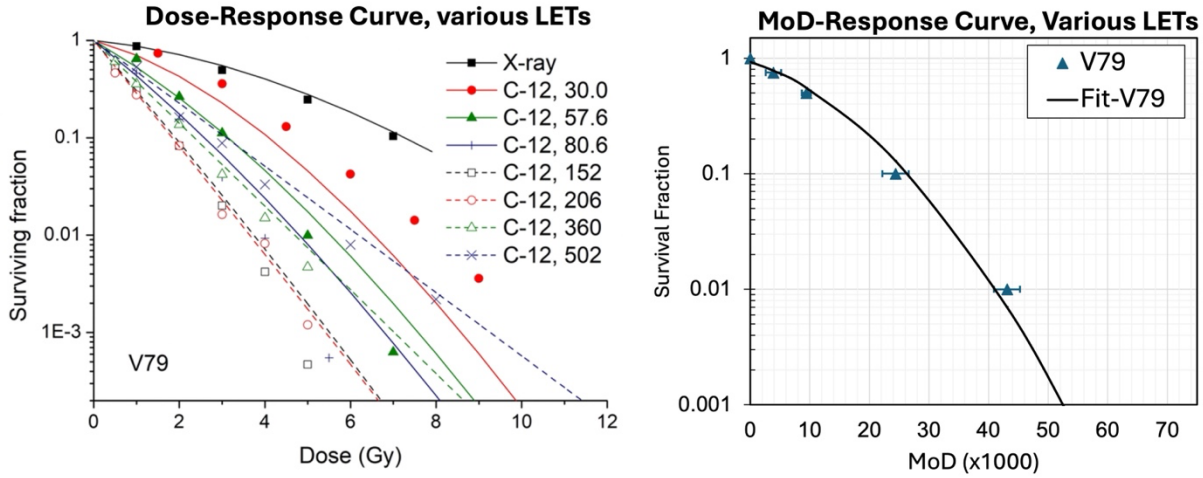
Purpose: Biological effects of ionizing radiation are primarily assessed based on absorbed dose, measured in Gray (Gy). However, the Gy is fundamentally inadequate for differentiating LET-dependent physico-chemical and biological processes, necessitating the use of empirical dose modifiers like RBE or quality (Q) factors. These modifiers are empirical factors that neither generalizable nor predictive across different radiation types. To overcome these limitations, we introduce the Molecular Dosimetry Unit, termed MoD, a novel framework designed to bridge energy deposition with biological responses by quantifying radiation-induced DNA alterations in a cell-free system.

Methods: The MoD is defined as the product of the Clustered Alteration Size (CAS) and Clustered Alteration Frequency (CAF). CAS represents the probability of radiation-induced molecular alteration, while CAF captures the frequency of CAS occurrence within a biomolecular dosimeter with specific material composition. CAS and CAF were modeled in an 8-μm^3 volume composed on $2.2x10^8$ nanometric voxel containing 15 base-pair of hydrated DNA (22 H_2O/nucleotide). MoD was determined by mapping the reactive species generated in the nano-voxels using Monte-Carlo simulation to the measured yields of DNA lesions. A cell-free environment isolated primary damage from confounding cellular repair mechanisms. The utility of MoD was evaluated by re-analyzing published cell-survival data for various animal and human cell lines across a broad LET range (1.0–5000 MeV·cm2/g) including electrons, protons, alpha particles, and carbon ions.

Results: The MoD importantly consolidates disparate, LET-dependent cell survival curves into a single unified curve for each cell line, inclusive of dose, particle type, and LET (Figure 1). This capability of MoD eliminates the need for empirical RBE and Q factors. Application of the MoD in depth-dose and spread-out Bragg peak (SOBP) reveals significant deviations from dose profiles. While the dose remains constant within SOBP region, the depth-MoD distribution increases with depth and peaks at the distal edge (Figure 2), capturing the biological impact of increased LET.

Conclusions: The MoD establishes a dosimetry framework inclusive of radiation type, dose, and LET for quantifying the biological effects of ionization radiation. This work supports the feasibility of a biomolecular metric to improve the prediction of biological effects in radiation medicine and protection without empirical RBE and Q factors.



Wang, W., *et al. Sci Rep* **8**, 16202 (2018).
Y. Furusawa, *et al. Rad Res*, 154(5), 485-496

Figure 1. Cell survival curves as a function of dose for various LETs of carbon ions and x-rays for V79 Chinese hamster cell line (left panel), and the re-plotting the same data as a function of MoD, resulting in the consolidation of all desperate curves into a single curve.

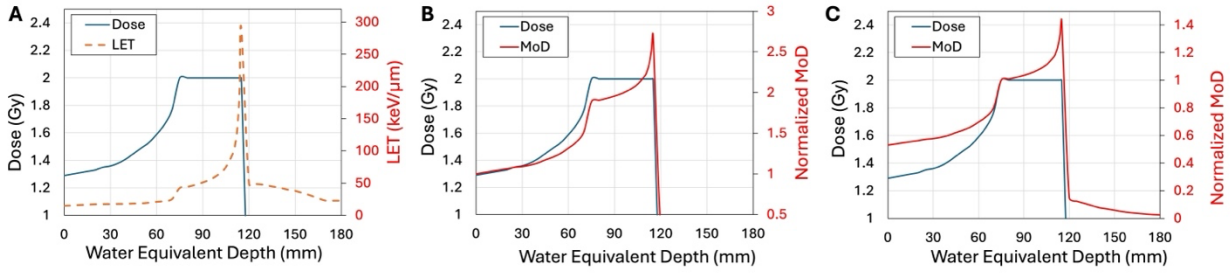


Figure 2. A 240 MeV/u carbon-ion beam delivering a uniform 2 Gy dose across a 4 cm SOBP*. (**A**) Depth–dose and LET distributions. (**B**) MoD-depth profile normalized to the phantom surface, shown alongside the depth–dose curve. (**C**) MoD-depth profile normalized to the proximal edge of the SOBP, shown alongside the depth–dose curve.

*Depth-dose and LET data are adapted from Int J Rad Oncol Biol Phys, 121(5), 1282−1292, 2025