The role of recoiled nuclei effective RBE in equivalent dose estimation for Alpha DaRT (^{224}Ra) dosimetry

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INTRODUCTION

The relative biological effectiveness (RBE) of high-LET recoil nuclei from the ^{224}Ra decay chain has not previously been studied in the context of diffusing alpha-emitters Radiation Therapy (Alpha DaRT). The RBE of heavy ions is known to saturate at high-LET values due to the *"overkill effect,"* where further increases in ionization density result in wasted energy deposition rather than enhanced biological damage relative to a reference photon beam. This study aims to clarify if recoil nuclei have the potential to contribute significantly to the equivalent dose deposited by Alpha DaRT sources.

METHODS AND MATERIALS

Innovation/Impact: According to recent studies [1,2], the RBE for high-LET ions can reach ~1.06 at LET ≃ 2000 keV/µm. We present a quantitative estimation of the effective RBE of recoiled nuclei (RBE_{Eff}), primarily originating from ^{212}Pb progeny, accounting for both their intracellular biodistribution probabilities and energy deposition characteristics. As a worst-case scenario, we used parameters based on a previous study by Azure *et al.* [3] using γ-ray spectroscopy measurements with an HPGe detector for the radiochemical dipyrrolidine-dithiocarbamato-^{212}Pb(II) in V79 cells. They found that approximately 72% of the intracellular activity of ^{212}Pb(PDC)$_2$ localizes within the cell nucleus ($P_{nucleus}$), and about 35% of this nuclear dose fraction is bound to nuclear DNA (P_{DNA} ≃ 0.35). An effective RBE for the recoiled nuclei can be defined as:

$$RBE_{Eff} \approx F_{Dose} \times P_{cell} \times P_{nucleus} \times P_{DNA} \times RBE$$

where F_{Dose} is the dose fraction, defined as the ratio of the dose deposited by recoiling ^{212}Pb decay progeny (^{212}Bi, ^{208}Tl, ^{212}Po, and stable ^{208}Pb) to the total dose from all recoiling nuclei. This fraction is a function of the radial distance from the Alpha DaRT source. The variable P_{cell} is defined as the fraction of ^{212}Pb present in the tissue that is taken up by cells.

RESULTS

The dose fraction of ^{212}Pb progeny localized within the cell volume is illustrated in Figure 1(a), and the RBE_{Eff} is shown in Figure 1(b), assuming $P_{cell} = 1$ (as a high value estimate of RBE_{Eff}).

Furthermore, the radial dose profiles in Figure 2 show that, although recoiling nuclei contribute to the total physical dose, their radiobiological equivalent dose remains significantly lower due to the low RBE_{Eff}, which varies with radial distance *r*. This indicates that, at extremely high LET values, the biological effect does not scale linearly with the physical dose.

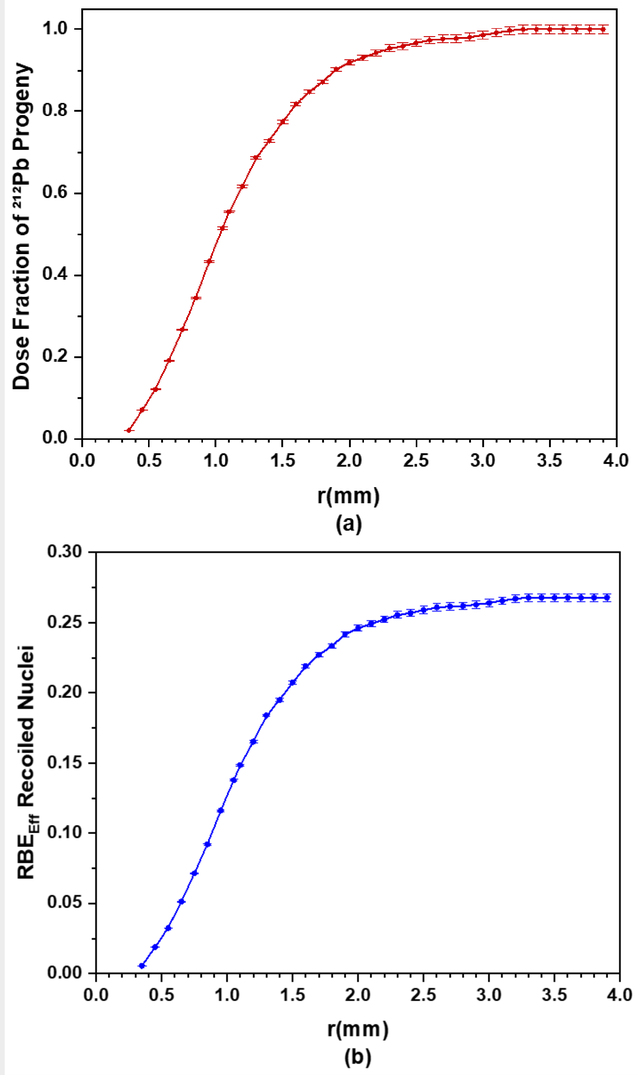

Figure 1: (a) The dose fraction of ^{212}Pb progeny, and **(b)** the RBE_{Eff} of recoiled nuclei as a function of the radial distance r from an Alpha DaRT source.

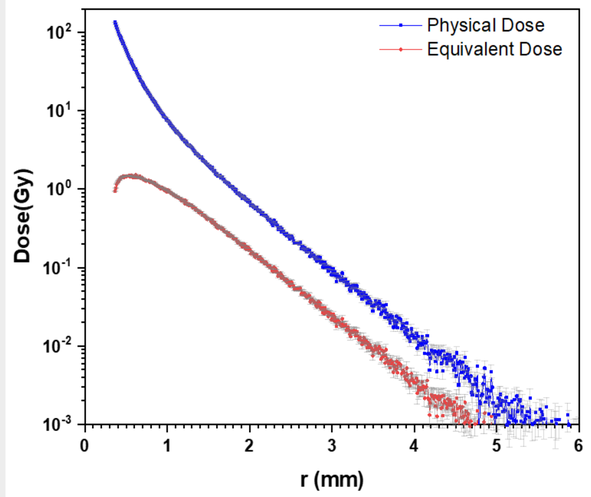

Figure 2: Radial profiles of the physical dose deposited by recoiling nuclei and the corresponding equivalent dose.

DISCUSSION

This study demonstrates that recoiled nuclei contribute negligibly to the Alpha DaRT therapeutic effect. The observed RBE_{Eff} is remarkably low (despite high LET values) partly due to the "overkill effect," where a very high energy deposition density yields a diminishing radiobiological effect (RBE ~ 1.06). Furthermore, the extremely short range of these nuclei means they must be localized within the cell nucleus to cause DNA damage. Since Alpha DaRT lacks chemical ligands for nuclear targeting, the recoil energy is primarily dissipated in non-critical regions. Therefore, our findings suggest that for clinical dosimetry based on equivalent dose estimation, the effective radiobiological contribution of recoiled nuclei can be safely neglected compared to the one of alpha and beta particles.

CONCLUSIONS

Results show that RBE_{Eff} varies between 0.005 and 0.268, reaching its maximum beyond 3.4 mm from the source. More importantly, Alpha DaRT therapy does not involve the use of a targeting ligand (like PDC) whose function is to promote intracellular and intranuclear uptake. As noted by Azure *et al.* [3], if the PDC ligand is lost, recoil energy is dissipated entirely outside the cell nuclei, resulting in an almost negligible radiobiological effect. Consequently, while recoiled nuclei contribute to the physical dose deposited in tissues, they do not play a significant role in the radiobiological equivalent dose.

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