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Original article

# Normal cell responses to 3D-CRT, VMAT, and helical tomotherapy: A comparative study



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#### ABSTRACT

*Objective:* To evaluate the dosimetric parameters and radiobiological effects in both irradiated and non-irradiated bystander cells of early- and late-responding normal tissues using three radiotherapy (RT) techniques: Three-dimensional conformal RT (3D-CRT), Volumetric modulated arc therapy (VMAT), and Helical Tomotherapy (HT).

Methods: HaCaT cells, representing early-responding normal tissue with a high  $\alpha/\beta$  ratio, and BEAS-2B cells, representing late-responding normal tissue characterized by a low  $\alpha/\beta$  ratio, were irradiated with a 2 Gy across three RT techniques. A water phantom was utilized for treatment planning to maintain uniform target coverage and ensure dosimetric comparability among all RT modalities. Various radiobiological endpoints were analyzed to assess cell responses in both irradiated and bystander cells.

Results: Although the dosimetric parameters ( $D_{95\%}\approx 2.0$  Gy,  $D_{2\%}\approx 2.1$  Gy,  $D_{mean}\approx 2.0$  Gy, HI = 0.04–0.35, beam-on time = 27–254 s, MU rate = 270–1936) were broadly comparable across the three RT techniques, the biological responses differed depending on cell type and irradiation method. HT irradiation induced the most pronounced cellular damage in HaCaT cells, with the survival fraction (SF) reduced to 0.31  $\pm$  0.09 in irradiated cells and cell viability of (93.5  $\pm$  3.7) % in bystander cells. In contrast, for BEAS-2B cells, VMAT predominantly affected irradiated cells (SF: 0.36  $\pm$  0.04), whereas bystander responses were more evident following HT irradiation [cell viability: (95.0  $\pm$  6.3) %]. These observations likely reflect an interplay between biological variables (such as, cellular phenotype, DNA repair capability, and cell cycle distribution), and physical parameters, including beam delivery characteristics, beam on time and MU rate.

Conclusion: These findings may help inform decision-making by radiation oncologists and support the development of individualized RT approaches aimed at maximizing treatment efficacy while minimizing long-term toxicity.

### 1. Introduction

The primary goal of radiation therapy (RT) is to deliver the highest effective dose to the tumor while limiting the dose delivered to surrounding organs at risk (OARs).<sup>1,2</sup> Nevertheless, some OARs, including nearby healthy tissues and adjacent organs may still receive radiation.<sup>3,4</sup> Advances in RT techniques such as intensity-modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT), and helical tomotherapy (HT), improve dose precision and better spare OARs compared to

conventional three-dimensional conformal RT (3D-CRT). <sup>1,2,5–8</sup> IMRT is an advanced RT technique that delivers highly accurate doses using computer-guided linear accelerators with varying beam intensities. <sup>5</sup> VMAT, an evolution of IMRT, provides continuous radiation during gantry rotation, dynamically adjusting intensity, beam shape, and speed, which enhances dose conformity and shortens treatment time. <sup>6</sup> HT combines computed tomography (CT)-based imaging with IMRT principles, delivering radiation in a helical trajectory coordinated with patient movement, offering high precision for irregularly shaped tumors while

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