Editorial

Cutting-edge technologies in external radiation therapy

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Radiation therapy (RT) is a key component of cancer treatment, complementing surgery and chemotherapy. While some technological advancements are still far from clinical application, others have been quickly adopted in the field of radiation oncology. This special issue features three reviews that highlight recent advancements in RT technologies, specifically particle therapy [1], FLASH RT [2], and artificial intelligence (AI) [3]. These articles also discuss the future prospects of these technologies.

Photons (X-rays) produced by linear accelerators (LINACs) are commonly used for the irradiation of tumors. However, the use of charged particles, such as protons and heavy ions (typically carbon), is on the rise [1]. The benefits of charged-particle therapy (CPT) stem from a physical phenomenon known as the Bragg peak. Unlike X-rays, which lose energy through attenuation as they pass through tissues, CPT allows the energy deposited per unit track to increase with depth. This results in a sharp and narrow peak of maximum energy deposition near the end of the particle's range. Consequently, the radiation dose delivered to the surrounding normal tissue is lower with CPT than with photons, offering better protection to organs at risk (OAR) located near the target.

Another advantage of CPT is that it interacts with cells differently than photons. Linear energy transfer (LET) is the amount of energy transferred by an ionizing particle to the material it passes through per unit of distance as it penetrates tissues. Heavy ions, such as carbon and helium ions, have a high LET. Radiation with high LET, like that from heavy ions, exhibits greater relative biological effectiveness (RBE) than low-LET radiation. The RBE for photons is set at a reference value of 1, while protons have an accepted RBE value of 1.1. Carbon ions, in contrast, can have RBE values ranging from 2.0 to 3.5. Despite these benefits, CPT has faced criticism for its high cost/benefit ratio, primarily due to its significantly higher costs and the lack of level-1 evidence compared to conventional photon treatments such as intensity-modulated radiotherapy (IMRT), which is commonly used to treat solid tumors. However, the growing number of CPT centers worldwide in recent years has led to an accumulation of clinical evidence suggesting that CPT can reduce toxicity and improve survival in selected cases.

Limiting toxicity to normal tissues has always posed a significant challenge in RT. FLASH-RT, an external beam RT technology, administers ultra-high doses in a very short duration [2]. Instead of administering treatment in multiple fractions over days or weeks, a large total radiation dose is delivered rapidly in a single fraction. Remarkably, these high dose rates (over 40 Gy per second) result in less damage to normal tissue compared to conventional dose rates (2–10 Gy per minute), while still preserving the radiation's ability to kill tumor cells. The underlying mechanism remains poorly understood. The most widely accepted theory for the FLASH effect is the oxygen depletion hypothesis, which suggests that the local oxygen depletion process occurs more quickly than reoxygenation during FLASH-RT. Consequently, normal tissue becomes more radioresistant under FLASH irradiation. This could represent a major advancement in RT; however, the clinical application of FLASH-RT still faces significant challenges and is far from routine use. Although initial results from animal and preclinical studies are promising, further research and clinical trials are necessary to translate these findings into effective cancer treatments.

In the field of radiation oncology, the application of AI is becoming increasingly widespread, with growing acceptance in clinical practice [3]. One of the most time-consuming aspects of the RT process is the segmentation or contouring of targets and normal structures in medical images, which is prone to significant intra- and interobserver variability. Deep learning models have significantly advanced as tools for the automated segmentation of OARs and are showing promise in contouring target volumes. Researchers are exploring the use of AI algorithms for automated treatment planning to reduce planning time, improve plan quality, and decrease interobserver variability. MRI offers superior soft-tissue contrast but lacks the electron density information required for RT planning. Deep learning models have been developed to generate CT images from MRI scans, and the resulting pseudo-CT images are useful for dose estimations in RT planning. Another emerging application of AI models is in predicting treatment outcomes. Traditional TNM prediction primarily focuses on cancer cells to forecast prognosis, but often falls short in accuracy. There is an increasing interest in employing radiomics signatures to predict overall and disease-free survival following cancer treatment. AI models have also shown potential in predicting RT-related side effects. The integration of AI with modern RT technologies could lead to significant transformations in the field of radiation oncology. However, there are ongoing concerns about the stability and generalizability of AI applications that need to be addressed before they can be fully integrated into clinical practice.

The authors of this special issue provide a comprehensive review of the recent developments and future prospects of these new technologies in radiation oncology.

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