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Perspective

Consequences of Radiation-Associated Carcinoma and Its Harmful Impact on Liver

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DESCRIPTION

Hepatocellular Carcinoma (HCC) is a type of liver cancer that is the fifth most common cancer worldwide and the third leading cause of cancer mortality. It is often caused by chronic infection with hepatitis B or C viruses, heavy alcohol use, obesity, diabetes, or exposure to toxins. HCC is usually diagnosed at an advanced stage, when surgical resection, transplantation, or ablation is not feasible or effective. Therefore, there is a need for alternative treatments that can improve the survival and quality of life of patients with HCC. One of the emerging options for treating HCC is irradiation, which uses high-energy rays or particles to kill cancer cells. Irradiation can be delivered externally by a machine (external beam radiation therapy) or internally by placing radioactive sources near the tumor (brachytherapy). Irradiation can be used as a primary treatment, a bridge to transplantation, an adjuvant therapy after surgery or ablation, or a palliative therapy to relieve symptoms.

However, irradiation for HCC poses several challenges, such as the risk of damaging the normal liver tissue, the heterogeneity and hypoxia of the tumor, and the resistance of cancer cells to radiation-induced cell death. Therefore, it is important to optimize the dose, fractionation, and delivery of irradiation to achieve the best balance between efficacy and toxicity. One of the advanced techniques that have been developed for irradiation of HCC is Stereotactic Body Radiation Therapy (SBRT), which delivers high doses of radiation in a few fractions with high precision and accuracy. SBRT has been shown to provide high rates of local control (89%-100%) and overall survival (30%-70% at 2 years) in patients with HCC. SBRT can also overcome some of the limitations of conventional irradiation, such as reducing the volume of normal liver exposed to radiation, increasing the tumor oxygenation, and enhancing the immune response.

However, there is no consensus on the optimal dose and fractionation scheme of SBRT for HCC, as different studies have used different criteria for patient selection, tumor size and location, liver function, and toxicity assessment. A recent multicenter study suggested that if tolerated by normal tissue, SBRT with a Biologically Effective Dose (BED) of 10 ≥ \u2009100 Gy (SaRT) should be used as a first-line ablative dose or SBRT with an equivalent dose in 2 Gy fractions (EQD2) ≥ \u200974 Gy (SbRT) Stereotactic Body Radiotherapy should be used as a second-line radical dose. Otherwise, SBRT with EQD2 <\u200974 Gy (ScRT) should be used as palliative irradiation. Another promising technique for irradiation of HCC is high Linear Energy Transfer (LET) radiation, such as heavy ions or protons, which have higher biological effectiveness than low-LET radiation, such as X-rays or gamma rays. High-LET radiation can cause more complex and irreparable DNA damage in cancer cells, leading to higher rates of cell death. High-LET radiation can also spare more normal tissue than low-LET radiation due to its physical characteristics, such as the Bragg peak and reduced lateral scattering.

Irradiation for HCC can also have beneficial effects beyond the local control of the tumor. For instance, irradiation can induce an abscopal effect, which is a systemic anti-tumor response triggered by local irradiation. Irradiation can also modulate the tumor microenvironment, which is a complex network of cells and molecules that influence the tumor growth and response to therapy. Irradiation can alter the tumor microenvironment by affecting the blood vessels, immune cells, fibroblasts, extracellular matrix, and cytokines. These changes can either enhance or impair the efficacy of irradiation or other therapies for HCC. Therefore, understanding and manipulating the tumor microenvironment is a potential avenue for improving the outcomes of irradiation for HCC.

CONCLUSION

However, high-LET radiation for HCC is still in its early stages of development and clinical application. There are limited data on its efficacy and safety in patients with HCC. Moreover, high-LET radiation is more expensive and less available than low-LET radiation. Therefore, more research is needed to compare the outcomes and costs of high-LET radiation versus low-LET

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radiation or other modalities for HCC. Irradiation is a valuable option for treating HCC in various clinical scenarios. However, it requires careful optimization and individualization to achieve the best results. Advanced techniques such as SBRT and high-LET radiation offer potential advantages over conventional irradiation but need further validation and standardization.