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Recent evidences of radiotherapy as a non-invasive ablation therapeutic option.

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Lecture : Hepatocellular carcinoma (HCC) patients mostly have an underlying chronic liver disease resulting from hepatitis B and C virus (HBV and HCV) infection, alcoholic liver disease, nonalcoholic fatty liver disease, etc. Intrahepatic disease progression is the main cause of death in non-metastatic HCC patients. Thus, effective local treatments in these patients are crucial. Various local treatment options for HCC patients, such as surgical resection, liver transplantation, local ablative treatments including thermal ablation and percutaneous ethanol injection (PEI), transarterial chemoembolization (TACE), radioembolization, etc., have been available, but many factors including tumor burdens, tumor characteristics, underlying liver function and patient comorbidities limit the treatment options.

With recent technological advances in radiotherapy (RT) and biologic understanding of liver tolerance to RT, modern sophisticated RT techniques, such as three-dimensional conformal RT, intensity-modulated RT and stereotactic body RT (SBRT)(1-4), have made it possible to deliver high doses of radiation to tumor(s) and reduce radiation doses to surrounding non-cancerous tissues including the remaining normal liver and gastrointestinal (GI) organs and these have shown promising outcomes in HCC patients with/without tumor vascular thrombosis (TVT). Compared with RT with X-ray, proton beam therapy (PBT), due to the inherent physical properties of the proton beam (called Bragg peaks), has an excellent depth dose distribution, which can increase the dose to the tumor while maintaining the radiation dose in the non-cancerous portion of the liver. Recently, PBT with various fractionations (i.e., 4 - 34 fractions) has been attempted and showed encouraging outcomes(5-11). Kim et al. (12) recruited 144 patients into a non-inferiority phase III randomised trial testing the hypothesis that proton beam radiotherapy (PBT) is non-inferior to radiofrequency ablation (RFA) in the treatment of patients with recurrent or residual HCC. Crossover was allowed if the assigned treatment was not technically feasible and occurred in 6 patients in the PBT arm and 19 in the RFA arm. The 2-year liver progression-free survival (LPFS) rate in the intention to treat population was 92.8% after PBT vs. 83.2% after RFA, meeting the criteria for non-inferiority. The 3- and 4-year LPFS rates were also non-inferior in PBT vs. RFA. Furthermore, in the per protocol population the 2-year LPFS rate was 94.8% after PBT and 83.9% after RFA. Common adverse events after PBT were radiation pneumonitis (32.5%) and leukopenia (23.8%), but no life-threatening adverse events were noted. These findings suggested that this new RT techniques, including PBT, is not inferior and can be applied safely in patients with small recurrent hepatocellular carcinoma.

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