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Stereotactic Body Radiation Therapy and Ablative Therapies for Solid Tumors: Recent Advances and Clinical Applications

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Using highly focused revolving radiation beams, stereotactic body radiation therapy (SBRT) can focus on tumor sites while minimizing the irradiation to the surrounding normal tissues, which is different from traditional radiotherapy.[1] Although it may cause difficult to manage toxicity, such as stenosis, ulceration, fibrosis, and even necrosis sometimes, it holds advantages such as high accuracy, noninvasiveness, and convenient outpatient treatment.[2] Similarly, Tumor ablation has been widely used in the clinical treatment of cancer because of its advantages of minimal invasiveness, high operability, and good repeatability. The most commonly used ablation methods are microwave ablation (MWA), radiofrequency ablation (RFA) and cry ablation, among which MWA and RFA belong to thermal ablation. In addition, irreversible electroporation may play an increasing role in the treatments of solid tumors.[3]

Stereotactic body radiation therapy, developed from stereotactic radiosurgery in the treatment of brain and spinal lesion, is commonly used in the treatment of early peripheral lung cancer and is increasingly used in the treatment of other primary or metastatic tumors.[4,5] Many studies were done to explore its application in early nonsmall-cell lung cancer.[6-10] Halperm *et al*[11] compared the toxicities and cost of proton radiation, intensity-modulated radiotherapy (IMRT), and SBRT among younger men with prostate cancer. They showed that SBRT and IMRT had similar toxicity, but SBRT was cheaper than IMRT. de Geus *et al*[12] evaluated the impact of SBRT on survival of patients with unresectable pancreatic cancer. Compared to chemotherapy alone or chemotherapy in combination with traditional fractionated external-beam radiotherapy, SBRT had a survival advantage. These results support SBRT as a promising treatment for patients with unresectable pancreatic cancer. Lazzari *et al*[13] evaluated SBRT for patients with metachronous oligometastatic ovarian cancer in reference to local control, toxicity, delay of systemic treatment, and survival outcomes. Results showed good local control with a favorable toxicity profile. Altogether, SBRT may be an attractive option for some cancers in specific clinical scenarios.

Ablation techniques have also made great progress in the treatment of solid tumors in recent years. For very early and early stage hepatocellular carcinoma (HCC), RFA has been recommended as a feasible alternative to surgical resection and liver transplantation. For HCC $\geq$2 cm, RFA combined with chemoembolization can contribute to near-curative therapy.[14,15] A Markov modeling study conducted by Pollom *et al*[16] showed that SBRT for initial treatment of localized, inoperable HCC was not cost-effective compared to RFA. However, SBRT is the preferred salvage therapy for local progression after RFA. Rajyaguru *et al*[17] analyzed the National Cancer Database and drew similar conclusions. In a study by Zhuo *et al*,[18] ultrasonographically-guided MWA was effective and safe for managing secondary hyperparathyroidism (SHPT) glands, providing rationale to use MWA for an alternative therapy for patients who are unable or refuse to undergo parathyroidectomy refractory or for patients having drug-resistant SHPT. Irreversible electroporation is a new tumor ablation technique that uses a pulsed electric field to create irreversible nanoscale pores on the cell membrane, thereby killing tumor cells. It has been attempted in liver tumor,[19-21] pancreatic tumor,[22-24] renal tumor,[25] among others. Furthermore, immunomodulatory drugs have the potential to enhance systemic anticancer immune effects induced by local thermal ablation, and several studies have investigated strategies for combining immunoadjuvants with thermal ablation to stimulate stronger

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antitumor responses with a hope for a systemic immune response.[3,26]

This Special Collection comprises 9 articles about the SBRT or ablative therapies for solid tumors, such as breast cancer, colorectal cancer, oral cancer, intracranial tumors, lung cancer, and liver cancer. Sutter *et al*[27] evaluated the feasibility, safety, and local efficacy of liver ablations assisted by a novel guiding tool—three dimensional (3D)-virtual target fluoroscopic display, which showed that 3D-virtual target fluoroscopic display improved visibility of tumors in recessed areas. Yuan *et al*[28] evaluated the efficacy and safety of transarterial chemoembolization (TACE) combined with RFA in the treatment of small HCC in special areas. They found that the combination of RFA and TACE appears to be effective and safe. Wang *et al*[29] assessed the overall survival (OS) and prognostic factors of laparoscopic MWA as a first-line treatment for HCC located at the liver surface infeasible for percutaneous ablation. They found laparoscopic MWA effective and well tolerated, and tumor number and ALT could be identified as independent predictors of reference-free survival while alpha fetoprotein (AFP) could be identified as independent predictor of OS. These results suggested that laparoscopic MWA could act as a treatment choice for patients with HCC with tumors at the liver surface improper for percutaneous approach. Studies conducted by Shen *et al*[30] investigated the effect of microwave-assisted liver resection for HCC, showing that MWA-assisted liver resection enabled liver resection with lower recurrence rate.

In regard to SBRT, Reynaud *et al*[31] investigated the safety and survival outcomes of hypofractionated stereotactic radiation therapy in the treatment for recurrent high-grade glioma. Hypofractionated stereotactic radiation therapy was well tolerated and provides an effective salvage option for recurrent high-grade gliomas with encouraging OS (15.6 months). Wee *et al*[32] compared the intra/interobserver variabilities of gross target volumes between computed tomography and magnetic resonance imaging in patients with lung cancer receiving SBRT.

Additionally, Li *et al*[33] investigated the prognostic value of pathologic features of oral squamous cell carcinoma in patients underwent seed implantation after radical surgery. They found that detailed microscopic description, particularly vascular infiltration, may help to identify patients who were more apt to tumor recurrence after treatment. Huang *et al*[34] explored the role of programmed death-1 (PD-1) in the recurrence of breast cancer after radiotherapy, showing that the recurrence-free mean survival of PD-1 low expression group was significantly longer than that in PD-1 high expression group (68 vs 56 months). These results suggested that the expression level of PD-1 could be a potential prognostic biomarker for patients with breast cancer after surgery and radiotherapy.

Although some studies in this Special Collection may have some shortcomings, such as retrospective nature, single-center observation, and selection bias, we can still get some clinical advice from these studies. Nonetheless, we are yet on the way to get better evidence on the safety, efficacy, and indications of SBRT and ablative therapies for patient with solid tumors.

Authors' Note

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