

Adding immunotherapy to RFA may benefit colorectal cancer patients with liver metastasis

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Radiofrequency ablation (RFA), a procedure to treat liver metastases in patients with colorectal cancer, was found to induce antitumor immune responses in human samples of primary colon tumor, and mice treated with a combination of RFA and an immune checkpoint inhibitor survived longer than those treated with either one of the two therapies, according to a study published in *Clinical Cancer Research*, a journal of the American Association for *Cancer Research*.

"Liver is the most common site of [colorectal cancer](#) metastasis, and about 20 percent of colorectal cancer patients have [liver metastases](#) at the time of diagnosis [synchronous liver metastases]," said Binfeng Lu, PhD, an associate professor in the Department of Immunology at the University of Pittsburgh.

Resection of liver metastases first (liver-first approach) is considered the best option for patients whose hepatic disease is predominant and if the primary [tumor](#) is asymptomatic or if symptoms are easy to manage, Lu explained. For these patients, RFA, a procedure that uses electrical energy to destroy cancer cells, is recommended as an alternative to surgery of the liver metastases, especially if the liver nodules are small.

"RFA is mainly recommended as local treatment for its physical effect of tumor destruction presently, and its immune effect has not been well studied. Our study revealed that RFA elicits systemic antitumor

responses, and combining this with immune checkpoint blockade can potentially unleash the powerful immunotherapeutic effect of RFA," Lu said.

Lu and his team, in collaboration with researchers from Soochow University in China, including Changping Wu, MD, PhD, Jingting Jiang, MD, PhD, and Liangrong Shi, MD, PhD, analyzed colorectal tumor samples collected from 78 patients with liver metastases admitted to the Third Affiliated Hospital of Soochow University. Of these patients, 38 received RFA of liver metastases before their primary colorectal tumors were treated.

The researchers found that RFA treatment of liver metastases increased the infiltration of T cells in the primary colon tumor, and that it also increased levels of the immune-inhibitory molecule PD-L1 in tumor cells and immune cells within the tumor.

"These studies show that liver RFA results in systematic inflammatory responses in the primary colon tumors and makes them more accessible to T cells. These properties of RFA suggest it can potentially be used to make colorectal cancer patients who are nonresponsive to PD-1-based immunotherapy become responsive," Lu said.

The researchers then conducted experiments in mice and found that an anti-PD-1 antibody was effective in inhibiting the RFA-induced PD-L1 upregulation, and a combination of RFA and PD-1 blockade was more potent than RFA or PD-1 blockade tested individually.

"These studies suggest that RFA complements and synergizes with anti-PD-1 immunotherapy," Lu said. "As immune checkpoint inhibitors become available to colorectal cancer patients in the clinic, RFA might be used as adjuvant immunotherapy in patients with multiple metastases."

The investigators are planning to initiate a phase I clinical trial to evaluate the efficacy of combination therapy with RFA and anti-PD-1 antibody for patients with liver metastases from colorectal [cancer](#).

More information: PD-1 Blockade Boosts Radiofrequency Ablation–Elicited Adaptive Immune Responses against Tumor. *Clin Cancer Res* March 1, 2016 22:1173-1184; [DOI: 10.1158/1078-0432.CCR-15-1352](#)

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