Lay Abstract:

Liver-dominant metastatic breast cancer (LMBC) poses a significant clinical burden, characterized by a poor prognosis and limited therapeutic options. Current therapeutic approaches primarily rely on systemic chemotherapy. Recent advancements in immunotherapy, particularly the introduction of immune checkpoint inhibitors targeting programmed cell death protein 1 (PD-1) and programmed death-ligand 1 (PD-L1), have shown promise in select breast cancer subtypes. However, their effectiveness in LMBC remains constrained by various factors, including the liver's unique microenvironment and its role in systemic immune regulation.

In this context, the proposed research seeks to overcome these barriers by combining immune checkpoint inhibitors with hepatic radioembolization. Radioembolization, utilizing yttrium-90 (90Y) microspheres, delivers localized radiation to liver tumors, sparing non-malignant tissue. This targeted approach has shown efficacy in LMBC, eliciting tumor responses and improving survival rates. Furthermore, preclinical and early clinical evidence suggests that radiotherapy-induced immune modulation can synergize with immunotherapy, potentiating anti-tumor immune responses. By leveraging the innovative combination of immune checkpoint inhibitors with hepatic radioembolization, the study aims to revolutionize therapeutic paradigms and improve patient outcomes.

The study's research plan aims to elucidate the immunological mechanisms underlying the synergistic effects of radioembolization and immune checkpoint blockade in LMBC. Through analysis of tissue biopsies and peripheral blood samples, the researchers seek to delineate immune alterations within the liver microenvironment and systemic immune activation. These insights hold immense potential for informing novel therapeutic strategies and advancing personalized medicine approaches in LMBC management.