Modeling pancreatic cancer dynamics with immunotherapy

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We develop a mathematical model of pancreatic cancer that includes pancreatic cancer cells, pancreatic stellate cells, effector cells, tumor promoting and tumor suppressing cytokines to investigate the effects of immunotherapies on patient survival. The model is first validated using the survival data of two clinical trials. Local sensitivity analysis of the parameters indicates there exists a critical activation rate of pro-tumor cytokines beyond which the cancer can be eradicated if four adoptive transfers of immune cells are applied. Optimal control theory is explored as a potential tool for searching the best adoptive cellular immunotherapies. Combined immunotherapies between adoptive ex-vivo expanded immune cells and TGF-β inhibition by siRNA treatments are investigated. This study concludes that mono-immunotherapy is unlikely to control the pancreatic cancer and combined immunotherapies between anti-TGF-β and adoptive transfers of immune cells can prolong patient survival. We show through numerical explorations that how these two types of immunotherapies are scheduled is important to survival. Applying TGF-β-inhibition first followed by adoptive immune cell transfers can yield better survival outcomes.