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Minimally invasive ablative therapy for mucinous cystic neoplasms (MCN) in a genetically engineered mouse model

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Pancreatic cystic neoplasms are an increasing health problem in the adult population due to their inherent potential to progress to invasive adenocarcinomas. The only available treatment is surgical resection with the consequential significant morbidity and mortality associated with pancreatic surgery. Direct injection of an ablative substance represents a potential new approach to this problem. Limited studies performed in human subjects speak to the potential feasibility of this approach (Oh et al., 2008 and DeWitt et al., 2010), but no systematic or rigorous assessment of agents and outcomes has been possible. We proposed to study the effectiveness of intracystic injections of different ablative substances and chemotherapeutic drugs for the treatment of mucinous cystic neoplasms (MCN) in a murine model of the disease. We have developed a genetically engineered mouse model of MCN (*Kras*$^{LSL\text{-}G12D}$*Dpc4*$^{fl/fl}$*;Cre*) that recapitulates the prototypical features of the human correlate, including development of an ovarian-type stroma with estrogen receptor (ER) and progesterone receptor (PR) positive cells (Izeradjene et al., 2007). After identifying MCNs in the mouse, we have injected them with a chemical ablative regimens and conventional chemotherapies following cyst fluid aspiration. Disease response has been evaluated by high-resolution ultrasound and detailed histopathologic and molecular analyses has been performed on recovered tissues at study termination. The goal is to define the best therapeutic regimen for non-surgical management of MCNs for a future clinical trial. Although we have been successful in identifying, aspirating and injecting the MCNs with saline (control) and also ablative substances including ethanol 98% under real time ultrasound guidance, there have been challenges including the difficult posterior localization of the treated lesions for histopathologic assessment in the diffusely abnormal pancreas typically found in this animal model. Potential solutions include comparison with direct visualization, ablation and marking of the cystic lesions on open surgery for histopathology analysis.