Introduction

In 2021, approximately 600,000 people will perish to cancer, and of those, 50,000 will be solely pancreatic cancer. Pancreatic ductal adenocarcinoma (PDAC) makes up 90% of all pancreatic cancer cases and is often diagnosed late stage due to its asymptomatic nature, causing the patient to have fewer options, most commonly leading to death, making it one of the deadliest forms of cancer. Currently, there are no diagnostic or imaging tools for early detection and this project intents to address this knowledge gap.

Experimental Methods

Genetically engineered mice (GEM), models (P48Cre:LSLKrasG12D; LSL-p53R172H (KPC)) with pre-invasive pancreatic intraepithelial neoplasia (PanIN) precursor lesions and control mice (P48:Cre or WT C57BL/6) without pancreatic lesions metabolic process were analyzed using hyperpolarized 1-13C pyruvate magnetic resonance spectroscopy (MRS). The dissolution dynamic nuclear polarization (DNP) operating at 3T was utilized to hyperpolarize 1-13C pyruvate. The 13C MRS of hyperpolarized 1-13C pyruvate were acquired at a 7T Bruker MRI scanner.

The biochemical development of alanine transaminase (ALT) and lactate dehydrogenase (LDH) enzyme activity were assessed. Afterward, deep learning (DL) techniques were implemented to develop a model and reveal hybrid biomarkers from the MRI and metabolic imaging to predict early detection of pancreatic cancer. The model was developed through Bayesian DL techniques and multi-modal data integration to allow uncertainty measurements and learn features from imaging modalities to consider improving prediction accuracy. After training the model, the learned features from multiple modalities to identify any correlation between MRI and metabolic imaging are explored that may lead to the discovery of new hybrid biomarkers with predictive values for the early detection.

Results

Hyperpolarized alanine-to-lactate signal ratio was found to decrease through progression from low to high-grade PanINs. These results demonstrate that there are significant alterations of ALT and LDH activities through the transformation from early to advanced PanINs lesions. Furthermore, we demonstrated that real-time conversion can be used as metabolic imaging biomarkers of pancreatic premalignant lesions, and the appropriate DL combining feature from the MRI and metabolic imaging as complementary modalities can lead to proper prediction of early detection in this KPC GEM model.

Conclusion

Findings from this emerging combination of DL and hyperpolarization-MRS techniques could potentially be translated into clinics for detection of pancreatic premalignant lesion in high-risk populations through early screenings with Figure 4 demonstrating the entire process more visually. Current efforts are ongoing to translate this technology at High-Risk Pancreatic Cancer (HR-PC) clinic at MD Anderson Cancer Center.

References