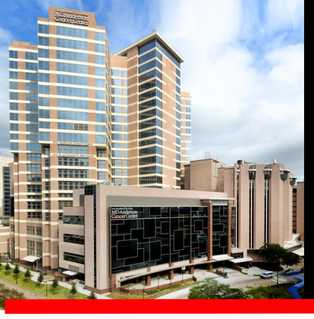

Early Detection of Pancreatic Cancer by Hyperpolarization and Artificial Intelligence

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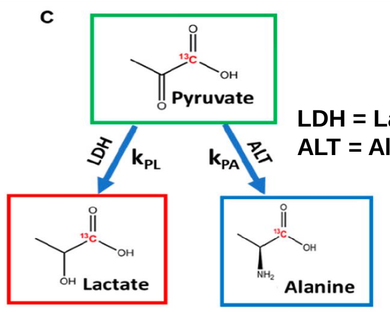
Introduction

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.

Figure 1

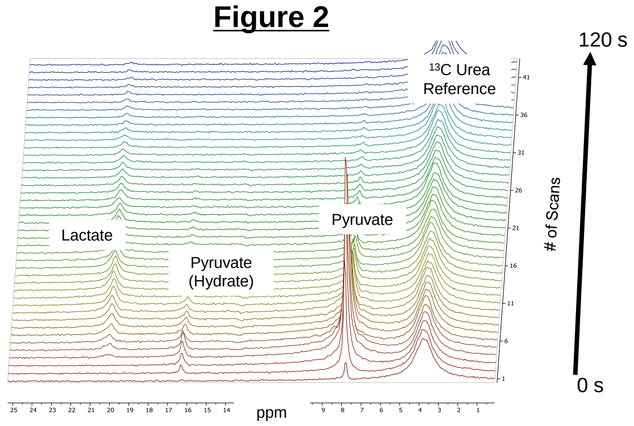


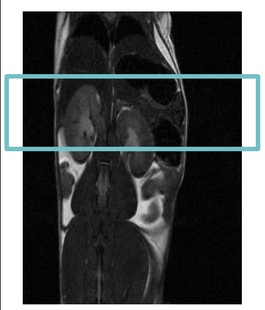
LDH = Lactate Dehydrogenase
ALT = Alanine Aminotransferase

An early-stage biomarker of biomarker of pancreatic cancer is the conversion of hyperpolarized (HP) pyruvate to lactate and alanine.

We are capable of monitoring this metabolic conversion rate employing hyperpolarized metabolic imaging. Employing hyperpolarized magnetic resonance (HP-MR) in unison with Artificial Intelligence (AI) to detect earlier premalignant stages of PDAC and even predict the efficacy of therapy in order to maximize treatment efficacy. HP-MR allows us to view the live metabolomics in the area of interest, in this case the pancreas.

Figure 2





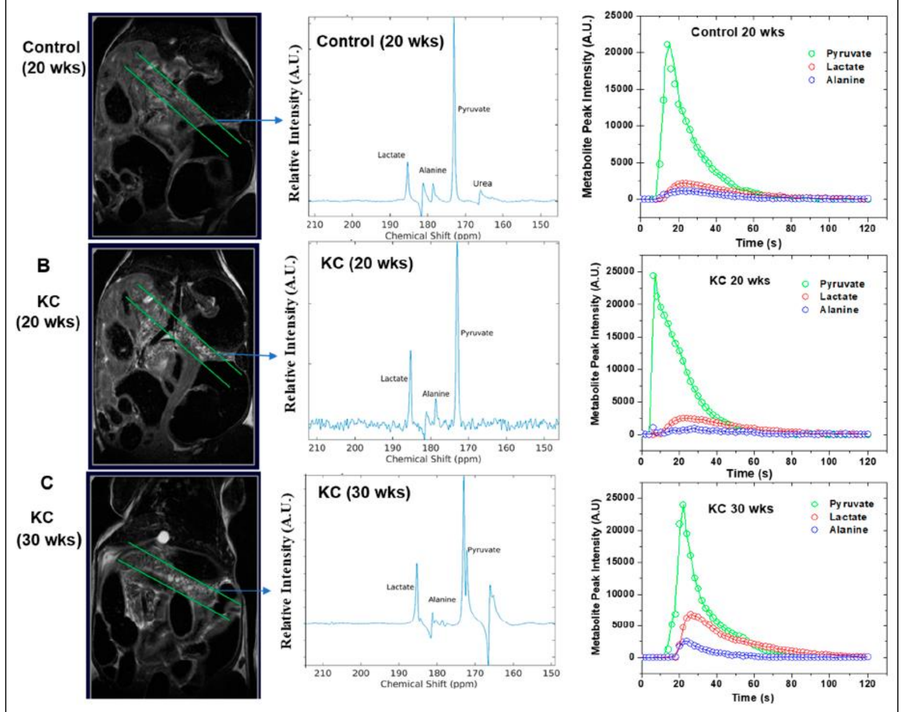
The live metabolic imaging is best displayed through MR spectroscopy (MRS) in which you can see real-time metabolic conversion. Through Deep learning (DL) applied to the AI, we can swiftly screen this data in order to catch a pre-indicator or see efficacy of treatment after detection.

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- ^{13}C pyruvate magnetic resonance spectroscopy (MRS). The dissolution dynamic nuclear polarization (DNP) operating at 3T was utilized to hyperpolarize 1-13C pyruvate. The ^{13}C MRS of hyperpolarized 1- ^{13}C 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.

Figure 3

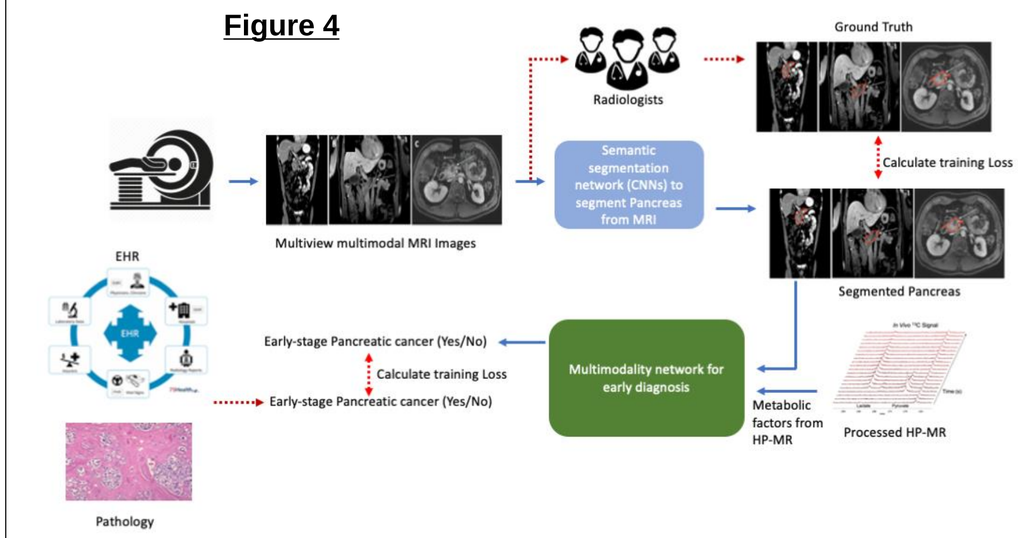


The real-time ^{13}C MR spectra were acquired in vivo following injection of hyperpolarized pyruvate. The lactate production was significantly higher in advanced time points. The mice were imaged at three different timepoints.

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.

Figure 4



A visual representation of the experimental method and outcome.

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.

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