

# Early Detection of Pancreatic Cancer by Hyperpolarized MRI

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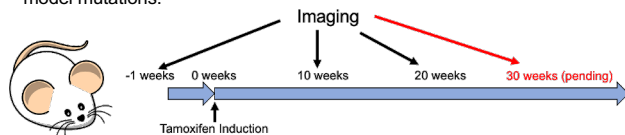
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## Objective

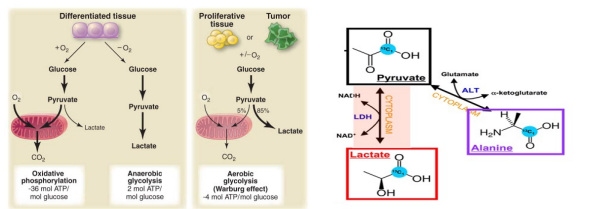
Currently, there are no diagnostic tools for the early detection of pancreatic cancer; therefore, the primary objective of this project is to develop and optimize a method of detecting premalignant stages of pancreatic cancer through hyperpolarized metabolic magnetic resonance imaging. This technique can increase the sensitivity of conventional magnetic resonance by over 10,000-fold, enabling real-time metabolic measurements. Hyperpolarized metabolic magnetic resonance imaging allows for non-invasive investigation of the metabolic flux as pancreatic cancer initiates and evolves *in vivo*.

## Methods

- Hyperpolarization experiments were performed with  $1\text{-}^{13}\text{C}$ -labeled pyruvate containing 15 mM trityl radical (OX63) using a commercial DNP polarizer (HyperSense, Oxford Instruments, UK) at 3.35T magnetic field and a temperature of 1.4 Kelvin.
- $^{13}\text{C}$ -spectra were obtained using a Bruker BioSpec 7T imaging scanner, which utilized a dual tuned ( $^1\text{H}$ ) volume coil and ( $^{13}\text{C}$ ) surface coil (Doty Scientific, SC). Area under the curve values were collected for each metabolite and lactate/pyruvate ratios were compared.
- Three different inducible mice models were used for these studies: P48CreERT2 (control), P48CreERT2:LSLKras (KC), and P48CreERT2:LSLKras:LSP53 (KPC). Mice were imaged at three time points: preinduction, 10 weeks, and 20 weeks.
- A tamoxifen induction system was implemented to regulate the mouse model mutations.



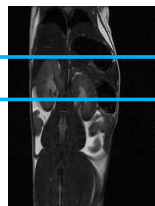
## Hyperpolarized $^{13}\text{C}$ Metabolic MRS/MRI



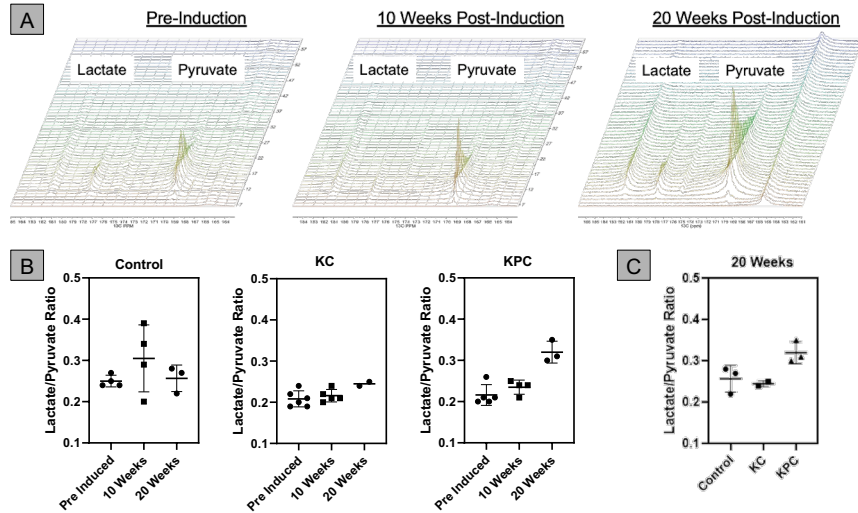
## Preliminary Data

Average ratio at time point	Control model (n)	KC model (n)	KPC model (n)
1 (14 weeks)	0.23672 (7)	0.248053 (3)	0.19819 (4)
2 (21 weeks)	0.144264 (7)	0.258622 (3)	0.336179 (1)
3 (28 weeks)	0.209469 (6)	0.258443 (4)	N/A

Previous research performed in our lab using a spontaneous mouse models (KC and KPC) it demonstrated a rise in the lactate/pyruvate ratio within the more aggressive KPC model; however, all KPC mice died prior to the third time point. Though the collected data is promising, we have since moved to an inducible model in order to have more control over the initiation of cancer, and thus providing better data.



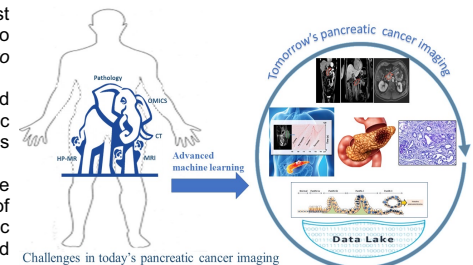
## Results



**Figure A:**  $^{13}\text{C}$ -spectra of KPC mice at preinduction, 10 weeks, and 20 weeks. As demonstrated on the right-most spectra, the lactate is higher in more advanced pancreatic cancer. Pyruvate to lactate conversion was visible lower at preinduction and 10 weeks. **Figure B:** Lactate/pyruvate ratio by mouse model. At 20 weeks, the KPC model showed a significantly increased ratio compared to the KC and control mice. **Figure C:** Mice model lactate/pyruvate ratio compared at 20 weeks. The more aggressive KPC model leads to a higher ratio, representing a more significant pyruvate to lactate conversion

## Summary / Future Direction

- Hyperpolarized  $^{13}\text{C}$ -MRS/MRI is fast becoming a real-time imaging modality to non-invasively follow metabolic fluxes *in vivo* for early detection of pancreatic cancer.
- Clinical translation of this technique could enable physicians to detect pancreatic cancer at a much earlier stage, thus improving patient outcomes and survival.
- At the MD Anderson Cancer Center, we are initiating a clinical trial for early detection of pancreatic cancer at the high-risk pancreatic cancer clinic by utilizing a recently installed clinical DNP polarizer.
- Our laboratory plans to collect data from one more time point (30 weeks) using these mice. We are also in the preliminary stages of incorporating Artificial Intelligence to our metabolic imaging modality for deep learning-assisted early detection of pancreatic cancer



## References

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