



Pancreatic Cancer Early Detection through Hyperpolarized MRI

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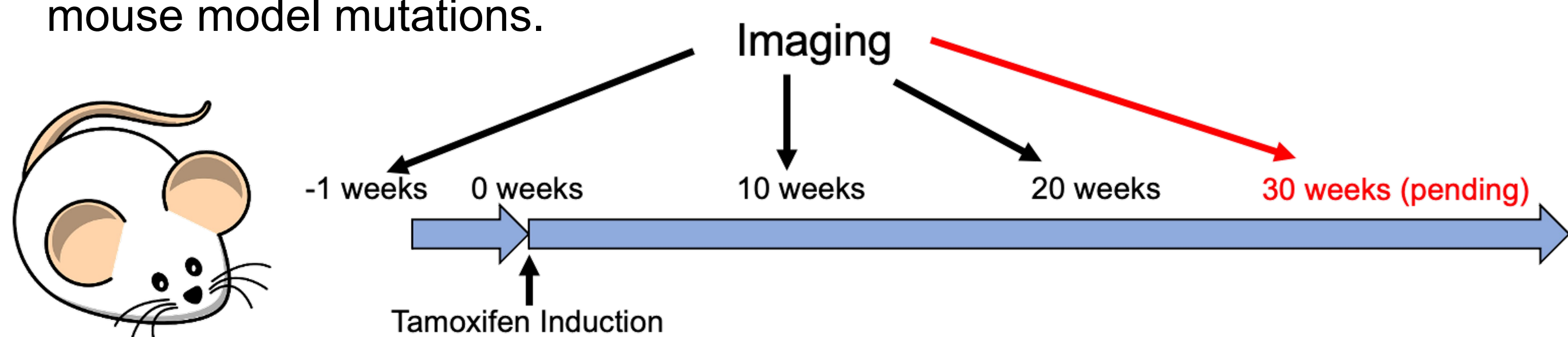
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Objective

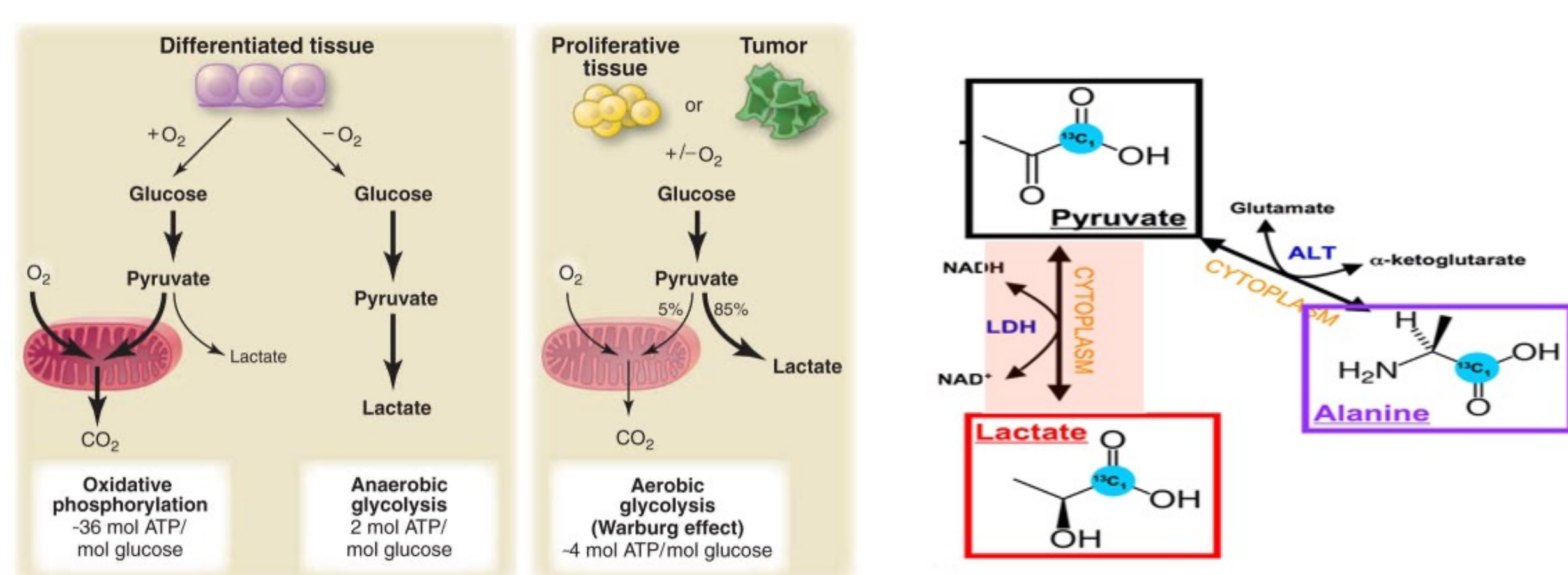
Pancreatic cancer is one of the most aggressive types of cancer with a 5-year survival rate of 11%, but with early diagnosis, the survival rate increases to 30%. At present, there are no diagnostic resources for early detection, thus through the use of Hyperpolarized MRI the objective of this project is to detect premalignant signs of pancreatic cancer. Hyperpolarized MRI imaging increases the sensitivity of magnetic resonance by 10000 times, allowing for non-invasive detection of altered metabolic pathways, a hallmark of cancer.

Methods

- The hyperpolarization experiments were performed with 1-¹³C-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.
- ¹³C-spectra were obtained using a Bruker BioSpec 7T imaging scanner, which utilized a dual tuned (¹H) volume coil and a (¹³C) surface coil (Doty Scientific, SC). Area under the curve values were collected for each metabolite and the lactate/pyruvate ratios were analyzed.
- We used three different inducible mice models for these studies: P48CreERT2 (control), P48CreERT2:LSLKras (iKC), and P48CreERT2:LSLKras:LSLP53 (iKPC). The mice were imaged at three time periods: preinduction, 10 weeks, and 20 weeks.
- A tamoxifen induction system was implemented to regulate the pancreatic mouse model mutations.



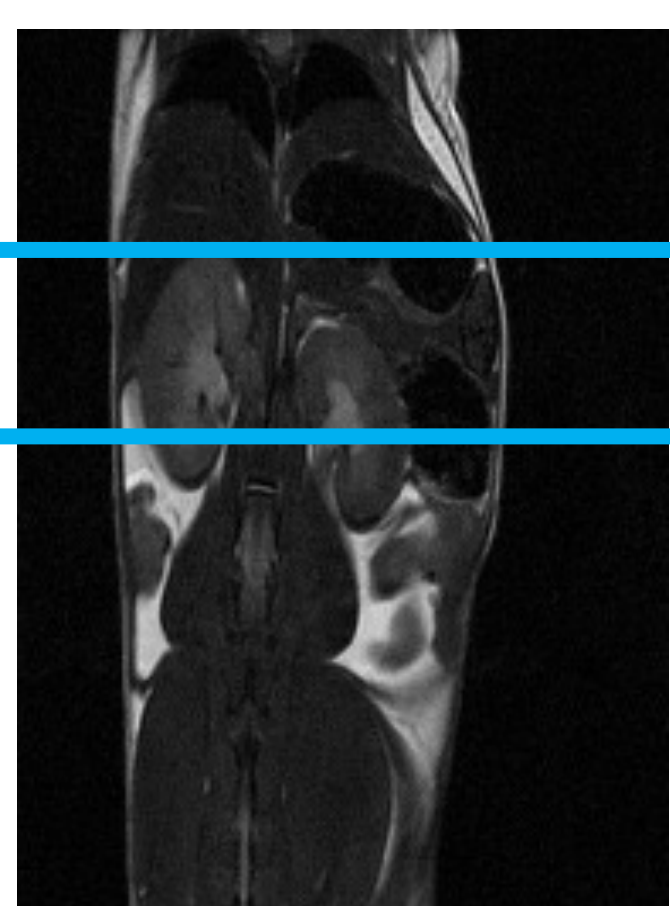
Hyperpolarized ¹³C Metabolic MRS/MRI



Preliminary Data

Average ratio at time point	Control model (n)	iKC model (n)	iKPC 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

In the early stages of this research, our lab previously used spontaneous mouse models, in which a pattern of increased lactate/pyruvate was observed in the iKC and iKPC models. However, by the 30-week incremental screening all of the iKPC models had died. Therefore, our lab has switched to induced mouse models, to have better control over cancer induction and imaging timepoints.



Results

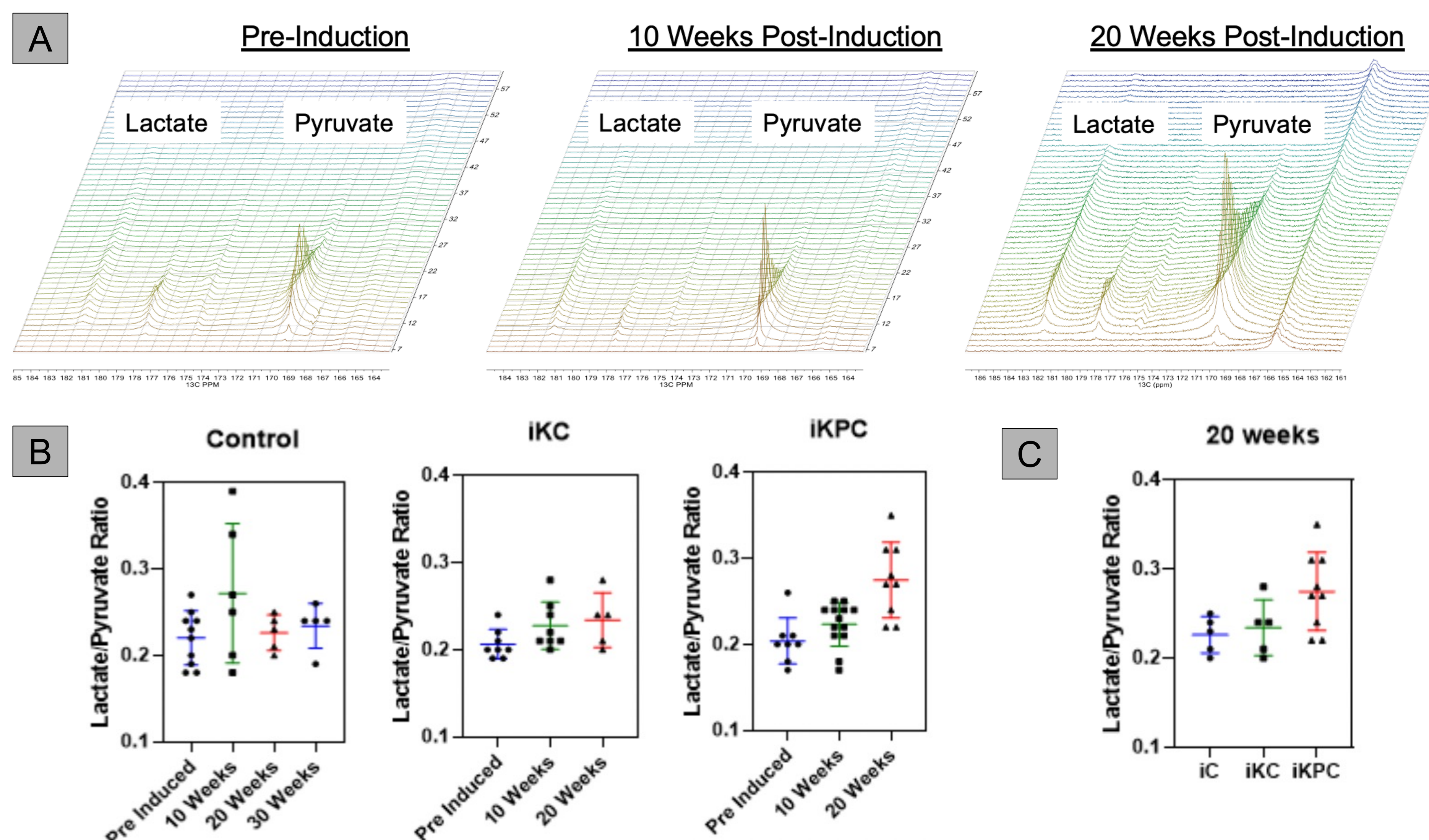
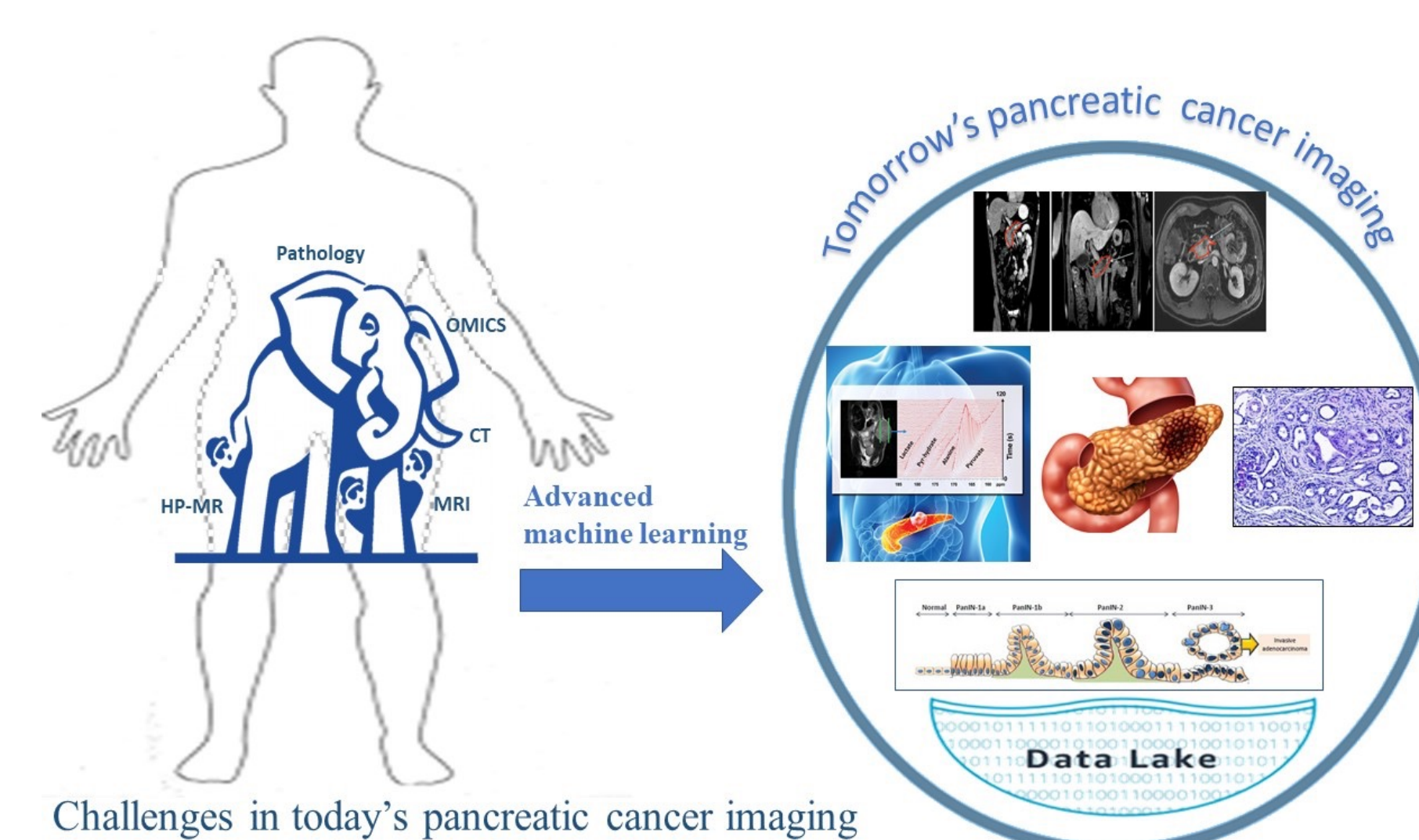


Figure A: This figure shows the ¹³C-spectra of iKPC mice at preinduction, 10 weeks, and 20 weeks. As demonstrated on the right-most spectra, the lactate is higher in more advanced pancreatic cancer cases. Pyruvate to lactate conversion was lower at preinduction and 10 weeks. **Figure B:** This figure displays the Lactate/pyruvate ratio by mouse model. At 20 weeks, the iKPC model showed a significantly increased ratio of Lactate/pyruvate compared to the iKC and control mice. **Figure C:** This figure shows the Mice model lactate/pyruvate ratio compared at 20 weeks. The more aggressive iKPC model leads to a higher ratio, representing higher pyruvate to lactate conversion.

Summary / Future Direction

- Hyperpolarized imaging enables noninvasive clinical diagnosis allowing for earlier detection of pancreatic cancer
- With the use of this imaging technique physicians will be able to detect pancreatic cancer earlier leading to higher chances of survival
- Our lab is currently beginning a clinical trial with the use of hyperpolarized MRI to detect pancreatic cancer earlier in the high-risk pancreatic cancer clinic
- We are planning on collecting data from one more increment at 30 weeks, to see the progression of the lactate/pyruvate ratio at later stages of pancreatic cancer in the mouse models
- Our laboratory is going to collect data from one more time period at 30 weeks using these mice models. We are also in the preliminary stages of incorporating Artificial Intelligence into our metabolic imaging modality for assisted early detection of pancreatic cancer.



References

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Responsible Conduct of Research:

For this research project, the Dr. Bhattacharya submitted a research protocol and obtained research approval from partner institutions.