Co-Clinical Quantitative Imaging of Small Cell Neuroendocrine Prostate Cancer Using Hyperpolarized $^{13}$C MRI

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This co-clinical study is aimed at developing comparable optimal murine HP $^{13}$C MRI protocols in realistic and representative models of small cell neuroendocrine prostate cancer bone and liver metastases to inform on therapeutic response using quantitative metrics to populate an online resource.
UCSF Team

- **Imaging protocols** - TCIA
- **Optimized imaging routines**
- **Modeling toolbox** - QIN
- **Online data and analysis portal** - CIRP
- **PDX models of metastases**
- **Integration of imaging & biological data** - OMF
- **Preclinical trial**
  - Drs. Peehl & Sriram
- **Clinical trial**
  - Drs. Kurhanewicz, Aggarwal & Ohliger
- **Informatics**
  - Drs. Larson, Sriram & Crane
- **Quantitative Imaging methods**
  - Drs. Larson & Sriram
- **Informatics**
  - Drs. Larson, Sriram & Crane
- **Quantitative Imaging methods**
  - Drs. Larson & Sriram
What is hyperpolarized 13C MRI?

Polarizer

Clinical Preclinical

Credits: Stanford.edu

What is hyperpolarized 13C MRI?

- Rapid dissolution methods
- Over 50,000-fold enhancement
- $T_1$-dependent signal decay
- Enables observation of dynamic enzymatic conversion

Credits: Stanford.edu

Project 1: Development of phantoms for testing rigor and reproducibility of hyperpolarized signal and kinetic modeling

Chemistry based

Enzyme based

Phantom layout with varying concentrations of enzyme, B) Measurement of hyperpolarized signal in LDH trapped alginate microspheres with 0.1 (blue), 0.25 (green) and 0.5 (red) kUnits.

3028 ROKET: a Robust Keto Enol Tautomerisation phantom for multi-site, multi-vendor hyperpolarized $^{13}$C studies

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https://index.mirasmart.com/ISMRM2020/PDFfiles/3028.html
Project 1: Development of phantoms for testing rigor and reproducibility of hyperpolarized signal and kinetic modeling

- **Goal:** Develop and test phantoms in clinical and preclinical polarizers for repetability

- **Encompasses:**
  - 3D printing
  - Basic biochemistry – enzyme kinetics isoforms, keto-enol tautomerization
  - Hyperpolarized $^{13}$C MRI
  - Kinetic Modeling
Project 2: Quantification of immunohistochemical stains

- Need: Correlate quantitative imaging metrics to molecular pathological markers

- Goal: Develop image processing algorithms to quantify expression of specific proteins from immune histochemical stains

- Encompasses:
  - Immunohistochemical stains
  - Clinical Pathology
  - Microscopy
  - Image Processing
Data Analysis

- Inputless unidirectional model to calculate $k_{PL}$ the apparent rate of conversion of pyruvate to lactate. Optimization of model and its parameters
  - Multi-compartment model

- Inclusion of vascular input function

- Impact of T1 values used for modeling

- Reproducibility
  - Robustness of model parameters using phantom
  - Evaluate intra and inter tumor variability

Imaging of patient-derived LuCaP93 SCNC cells in the murine tibia and liver. (A,D) T2-wt MRI shows the tumor in the left limb and liver (outlined in red). B) HP spectroscopic imaging shows the injected HP pyruvate and urea signal and the HP lactate produced from pyruvate in tumor voxel (orange square). E) Lactate signal dynamics observed in the liver tumor over time (black dots) was fitted using inputless model (red line) to yield a $k_{PL}$ of 0.11 s$^{-1}$ in the liver. (C,F) Calculated $k_{PL}$ map overlaid on the tumor.