Title: Clinical Imaging with Hyperpolarized C-13: The First Steps

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Highlights

- The feasibility and safety of metabolic imaging using hyperpolarized 13C pyruvate has been established for patients with prostate cancer
- Changes in 13C lactate/pyruvate highlighted regions that has been diagnosed as corresponding to cancer based upon prior biopsy

Target audience: This presentation is targeted to clinicians who are interested in the potential for using this new methodology and to scientists who wish to translate their pre-clinical findings into patient studies. It is anticipated that the audience will use the knowledge gained to understand the capabilities of the current technology, to assess the potential for future clinical applications and to appreciate where further advances are needed.

Study Description: The use of hyperpolarized agents is to improve the sensitivity and specificity for characterizing the malignant potential of tumors and to provide non-invasive imaging parameters that provide an early assessment of treatment efficacy in patients with cancer. This is an important problem because of the need to stratifying patients into cohorts more likely to respond to specific therapies and to make rapid decisions about whether the treatment is having the desired effect. The initial, dose escalation clinical trial of this technology was performed on 33 patients with prostate cancer with biopsy proven cancer being followed with active surveillance. Three doses were selected.

The hyperpolarized agent was prepared using a similar polarizer design and dissolution method to those applied in a pre-clinical setting [1] but with the entire process being performed in a clean room adjacent to the 3T MR scanner. An automated QC system was used to make sure that the final product met the specifications laid out in the IND. After successfully passing these tests, the sample was taken into the scan room, drawn into a syringe, injected into the subject and the MR scan performed. Custom designed 13C transmit and 1H/13C endorectal receive coils were used to perform dynamic 1-D or 2-D spectroscopic imaging (time resolution 3-5s) in some patients to determine the time course of delivery and metabolism, while single time point 2-D or 3-D spectroscopic imaging (Tacq= ~12s) provided finer resolution for study the spatial distribution of pyruvate and lactate signals in other patients.

The study was highly successful with no dose limiting toxicities and characteristic signals from pyruvate and lactate being observed at all three doses. The delivery of the agent was similar to that observed in previous pre-clinical models with lactate/pyruvate being elevated in the tumor relative to normal appearing prostate and in the vasculature surrounding the rectum. Although complex, the logistics of the examination worked well, with 31/33 patients receiving an injection and the 2 samples that were not injected being due to hardware issues rather than the polarization. The mean time from the agent being at 1.2K in the polarizer to it being in the patient was 67s and the signal persisted for a further 60-70s.

Next steps: A new polarizer design that provides simultaneous preparation of four 13C pyruvate samples and uses disposable sterile fluid paths has been developed [2] and is currently being tested to obtain the data for a revised IND in order to perform studies in new patient populations. The first trials with this system will be to look at reproducibility and response to therapy in populations of patients with prostate and brain cancers. As the technology is refined and becomes available for more widespread use a large number of different applications are envisaged, both with pyruvate and other hyperpolarized agents [3].

References:

1. Ardenkjaer-Larsen JH, Fridlund B, Gram A, et al. Increase in signal-to-noise ratio of > 10,000 times in liquid-state NMR. Proc Natl Acad Sci U S A 2003;100:10158-63.
2. Ardenkjaer-Larsen JH, Leach AM, Clarke N et al. Dynamic nuclear polarization polarizer for sterile use intent. NMR Biomed 2011;24:927-32.
3. Kurhanewicz J, Vigneron DB, Brindle K, et al. Analysis of cancer metabolism by imaging hyperpolarized nuclei: prospects for translation to clinical research. Neoplasia 2011;13:81-97