Hyperpolarzed 13C-1-Pyruvate Metabolic Imaging of Inflammatory Arthritis

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Introduction: Few quantitative methods exist to monitor the disease course of adult rheumatoid or juvenile idiopathic arthritis. Anatomic imaging tends to show late, less repairable stages. MRS imaging with hyperpolarized ^{13}C-1-pyruvate[1] ($H^{13}CP$) may provide an objective and quantitative measure of arthritis, which may be helpful in clinical decision making and treatment planning. The rational for imaging pyruvate is that energy metabolism is increased in inflammation and the rate of pyruvate metabolism may be upregulated in arthritic joints.[2,3] This work examines the feasibility of $H^{13}CP$ for detecting and characterizing arthritis.

Materials and methods: Arthritis was induced in the right hind paw or knee in 4 juvenile Sprague Dawley rats (age 4-6 wks, mean weight 134 g, range 96-165 g) by inj. of 0.4 μL/g complete Freund's adjuvant. Joints were imaged 7 d after induction with ^{13}C MRS on 3 T Signa™ MR Scanner (GE Healthcare, Waukesha, WI) equipped with self-shielded gradients (40 mT/m, 150 mT/m/ms). A custom-built dual-tuned (^{1}H/^{13}C) quadrature coil was used for both RF excitation and signal reception. $H^{13}CP$ was created by DNP technique, liquid state polarization=15-20%. 0.5-1 mL of 100mM $H^{13}CP$ was inj. via tail vein. Single-time point MRS was obtained 20 s after start of inj. with a FID CSI sequence (10mm sl thk, in-plane resol 2.5mmx2.5mm, FOV=4cmx4cm, 5 kHz spectral BW and 256 points). Time resolved imaging was obtained with a 1D EPSI sequence by projecting a 10mm slice onto 1D in left-right direction and applying an EPSI-flyback gradient trajectory to resolve spectroscopic signal (500 Hz, 32 points) in left-right direction (5mm resolution, 9cm FOV. Mean SI of pyruvate and lactate were obtained with ROI analysis at the joints. Normal and arthritic joints were compared with T-test.

Results: Arthritic joints showed redness and swelling, histological score=3 vs. normal=0 out of 4, and T_2W changes of arthritis on the anatomic ^{1}H images. ^{13}C-1-pyruvate and metabolized ^{13}C-1-lactate were increased at the arthritic joints on FID CSI images (Figure 1B, C). The ratios of metabolite to total ^{13}C signal showed trends towards significant differences for pyruvate: arthritic joints(AJ)=0.37 vs. norma(NL)l=0.29, p< 0.22 and lactate AJ=0.20 vs. NL=0.14, p<0.17. Although increased blood flow in inflamed tissue may account for the increased delivery of imaging agent, the rate of conversion to lactate also trended towards a significant increase in the arthritic joints as shown by time resolved imaging (Figure 2) and by the ratio of lactate to pyruvate: AJ=0.55 vs. NL=0.40, p<0.09.

Conclusion: Hyperpolarized ^{13}C-1-pyruvate imaging appears to show increased metabolism to lactate in joints affected by arthritis. Increased lactate production may serve as a marker of arthritis activity.

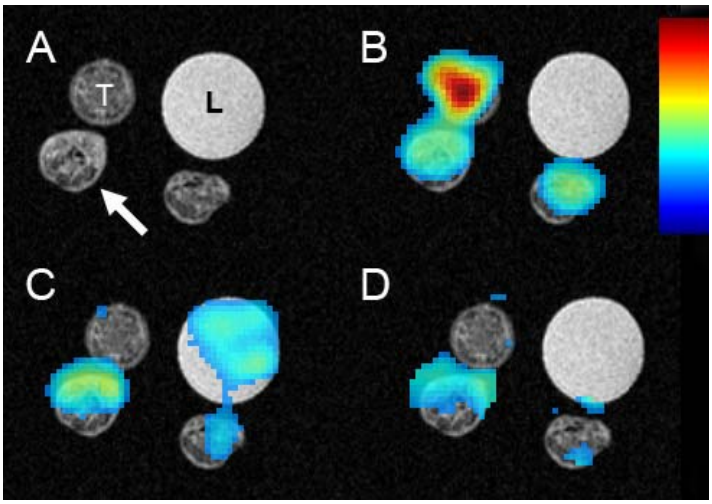

Figure 1. Metabolic maps at 20 s after inj. of $H^{13}CP$ demonstrate increased lactate production in the arthritic paw. A. T_2-weighted anatomic image shows tissue swelling at the arthritic right hind paw (arrow) in comparison to the normal left paw and is overlaid on the subsequent metabolic maps with tail (T) and non-polarized ^{13}C-lactate (L) reference tube. Maps show B. pyruvate, C. lactate, and D. the ratio of lactate to pyruvate.

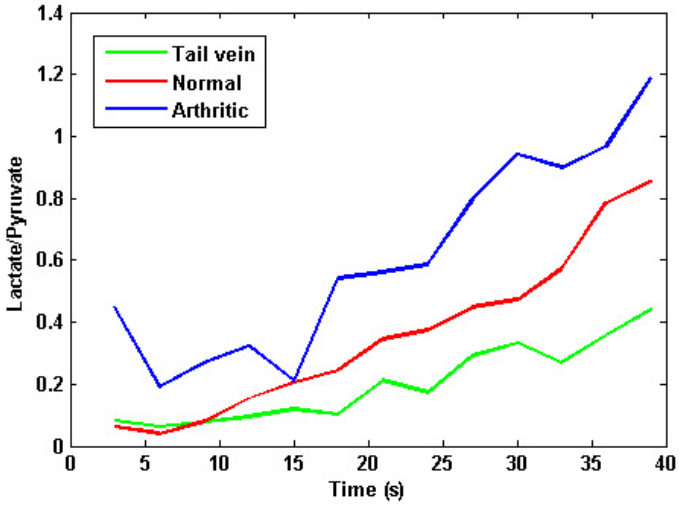

Figure 2. Time resolved imaging of one arthritic rat shows the increased production of ^{13}C-lactate in the arthritic paw (blue) in comparison to the normal paw (red) and tail (green).

References:

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