Hyperpolarised [1-^{13}C]-Pyruvate Metabolism in Brown Fat

Lanette J Friesen-Waldner[1,2], Trevor P Wade[1,2], Curtis N Wiens[3], Kundan Thind[1,2], Jacqueline K Harris[1], Kevin J Sinclair[1], Colin M McCurdy[1], Albert P Chen[4], Nica M Borradaile[5], and Charles A McKenzie[1,2]

[1]Department of Medical Biophysics, University of Western Ontario, London, Ontario, Canada, [2]Imaging Research Labs, Robarts Research Institute, London, Ontario, Canada, [3]Department of Physics and Astronomy, University of Western Ontario, London, Ontario, Canada, [4]GE Healthcare, Toronto, Ontario, Canada, [5]Department of Physiology and Pharmacology, University of Western Ontario, London, Ontario, Canada

Target Audience: This abstract is targeted to those interested in hyperpolarised ^{13}C MRI/S and/or obesity.

Introduction: Brown fat is adipose tissue that, in comparison to white fat, has multilocular lipid droplets, increased number of mitochondria, and is more metabolically active. Brown fat also has more vasculature due to its increased need for oxygen to support mitochondrial metabolism. It has been suggested that pharmaceutically increased brown fat metabolism may induce weight loss [1].

Purpose: To detect metabolism in brown fat using hyperpolarised [1-^{13}C]pyruvate magnetic resonance spectroscopy and ^{13}C chemical shift imaging.

Methods: 129/SVJ mice were fed a high fat diet (40% fat) for three months [2], under a protocol approved by the institution's Animal Use Subcommittee. Mice (N=2) were anesthetised using isoflurane and placed on a custom built surface ^{13}C RF coil inside a custom built switch tuned ^{13}C/^{1}H bird cage coil. ^{1}H MRI and ^{13}C MRS/CSI were performed in a 3T clinical MRI scanner (Discovery MR750, GE Healthcare, Waukesha, WI, USA). ^{1}H fat-water imaging was used to identify brown fat as described by Hu *et al* [3]. [1-^{13}C]pyruvic acid [Sigma Aldrich] was polarised using a DNP polariser (Hypersense, Oxford Instruments, Abingdon, UK). 250μL of the hyperpolarised solution (100mM pyruvate) was injected via the tail vein over 12s. Time resolved ^{13}C spectra (flip angle=10^{o}, readout filter=10,000Hz/4096 points, repetition time=3s, slice thickness=8mm) were acquired using a pulse-acquire pulse sequence with a slice-selective excitation pulse from the subscapular fat pad of the mouse. The slice was positioned obliquely to avoid the heart. 2D ^{13}C chemical shift images (FID-CSI, GE Healthcare) were acquired in an axial slice containing the subscapular fat pad (matrix=12x12, FOV=5cm, flip angle=10^{o}, 5kHz/256points readout, TR=160ms). CSI acquisition started 14s after the beginning of the bolus injection. Total scan time was 23s.

Results and Discussion: Similar results were obtained for both mice in this study. Fig 1 shows a representative plot of the time course of pyruvate and its metabolic products (alanine, lactate) obtained from an oblique slice through the subscapular fat pad of one of the mice. To minimise contamination of these spectra from signal outside the brown fat, 2D CSI was performed. Fig 2a shows the CSI grid overlaid on a fat fraction image for one mouse. Fat fractions from the voxels outlined in blue and red were 88±5% and 95±4% respectively, consistent with classification as brown fat (blue) and white fat (red). Spectra from these voxels (Fig 2b,c) show more metabolic activity (elevated lactate) in the brown fat voxel (Fig 2b) than the white fat voxel (Fig 2c). The ratio of lactate to total carbon was 53% in the brown fat, and 22% in the white fat.

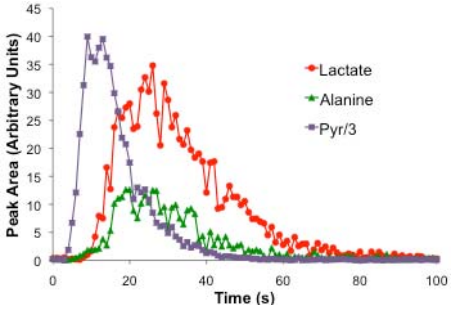

Fig 1: Time course of peak intensities from the dynamic spectra obtained from an oblique slice through the subscapular fat pad of a mouse.

Conclusions: Using ^{13}C CSI, more metabolism of [1-^{13}C]pyruvate to lactate was seen in brown fat than white fat. These results suggest that hyperpolarised [1-^{13}C]pyruvate MRS and CSI can be used to differentiate the metabolic activity of brown fat from white fat.

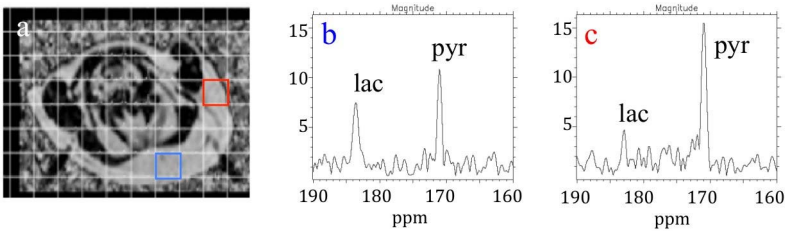

Fig 2: a) 2D CSI overlaid on the fat fraction image. b and c) The CSI spectra from the brown (blue ROI) and white (red ROI) fat, respectively. There is increased conversion of pyruvate (pyr) to lactate (lac) in the brown fat spectrum.

Acknowledgements: We acknowledge support from GE Healthcare, NSERC, the Ontario Research Fund and the Canada Research Chairs Program.

References: [1] Tam *et al.* Circulation 2012;125:2782. [2] Syn WK *et al*. Liver Int 2009;29(8):1262. [3] Hu *et al.* JMRI 2010;31:1195.