



Cardiac MRI

$^{13}\text{C}$ -Lactate

$^{13}\text{C}$ -Bicarbonate

*In vivo*, cardiac  $^{13}\text{C}$ -MR images, acquired following infusion of  $[1-^{13}\text{C}]$ pyruvate, overlaid on reference anatomical image

- $^{13}\text{C}$ -lactate image shows the lactate dehydrogenase (LDH)-mediated conversion of pyruvate into lactate.
- $^{13}\text{C}$ -bicarbonate image shows the flux of pyruvate through pyruvate dehydrogenase (PDH)

I gratefully received my ESC First Contact Initiative Grant in October 2012, and used it to facilitate a three-week-long trip to visit the University of California San Francisco in November 2012. My goals while at UCSF were two-fold: 1) to set up new methods for imaging metabolism in the *in vivo* mouse heart, using hyperpolarized  $^{13}\text{C}$ -labelled tracers in concert with magnetic resonance imaging and spectroscopy (MRI and MRS) at 14 T, and 2) to meet with and present my work to individuals in the departments of cardiology and radiology who may be able to help in my efforts to obtain NIH research funding and a tenure-track faculty position at UCSF in the near future.

My work setting up mouse heart metabolic MRI at 14 T proved very successful. While metabolic MR using hyperpolarized  $^{13}\text{C}$ -labelled tracers has shown great promise to investigate and diagnose heart disease in rats, large animals and even in people, the ability to acquire reliable data from the mouse heart has been limited due to the challenges of the animal's small size the rapid heart rate. This has obviously been a major limitation in using the technology to determine the effect of genetic manipulations on cardiac physiology. At UCSF, I was able to set up cardiac gating to enable acquisition of proton MR images for structure/function measurements and image registration. Furthermore, I was able to acquire  $^{13}\text{C}$  images of the [1- $^{13}\text{C}$ ]pyruvate derived metabolites [1- $^{13}\text{C}$ ]lactate,  $^{13}\text{C}$ -bicarbonate and [1- $^{13}\text{C}$ ]alanine: the first of their kind. These images were acquired using a GRASE (gradient and spin echo)-based sequence developed in house, which imaged each resonance of interest serially within 150 ms (i.e. on par with the R-R interval corresponding with the murine heart rate). In future, this sequence can be easily modified to image metabolites arising from different input metabolic tracers (such as imaging glutamate and acetylcarnitine derived from [2- $^{13}\text{C}$ ]pyruvate, or imaging the redox-dependent ratio between dehydroxyascorbate and ascorbate). I plan to use these techniques, collectively, to measure cardiac metabolism in transgenic mice and mice subjected to an ischemia-reperfusion model of heart disease.

My goal of making contacts to facilitate tenure-track employment at UCSF started out in a very promising manner, and indeed, while at UCSF I connected with numerous professors in both the radiology and cardiology departments and generated great interest in my work. For example, I gave a talk to Professor Dan Vigneron's group in radiology, scheduled a lecture I was to give to the Research Interest Group of cardiovascular radiologists, run by Professor David Saloner, and I met with the chief of cardiology, Dr Jeffrey Olgin, and arranged to give a talk to his research group. I also met with Professors Sarah Nelson and John Kurhanewicz, and participated in the organization of the High Field Cardiovascular Workshop run immediately before this year's Society of Cardiac Magnetic Resonance meeting in San Francisco.

However, during this time I also realized that moving to UCSF as the next stage of my career was not the best decision. The ESC First Contact Grant gave me the opportunity to experience an extended period of time in San Francisco, meeting my future colleagues, and experiencing the work environment at USCF, and as a result of this I was able to make a much more informed choice about where I will be able to thrive personally and professionally and have the most successful

career in science. Therefore, while in some ways the outcome of my trip to UCSF was a negative, I am exceptionally grateful for the insight it provided me with and the importance the trip was in my future development.

Looking forward, as a result of my ESC First Contact Initiative Grant, I have decided to remain in the UK (specifically in Oxford) to pursue my research, and will apply for future fellowship funding from organisations such as the Wellcome Trust and the British Heart Foundation. And the best part is, my experiences in setting up cardiac metabolic imaging in mice will be just as useful to me there as in San Francisco! Thank you once again to the ESC for providing me with the funding to have this formative and essential early career experience.