

Guest Talk: Dr. Michael Dodd

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From Mouse to Man: Cardiac Hyperpolarized Magnetic Resonance – Physiology and Pathophysiology

Cardiovascular disease (CVD) is the leading cause of death, with the World Health Organisation estimating 15 million deaths a year worldwide, roughly 27% of all deaths. A growing body of evidence places metabolic alterations at the heart of these conditions. A dysregulation in the finely tuned balance between fatty acid and glucose utilization has been shown to both be a cause of and consequence of physiological and pathophysiological alterations in the heart. The recent advances in cardiac hyperpolarized magnetic resonance spectroscopy (MRS) have allowed a greater understanding of the *in vivo* metabolic alterations that occur in the heart, and have facilitated a more detailed picture of the temporal nature of these changes. We have focused on a range of rodent models to understand metabolic alterations that are associated with CVD, before translating these into human volunteers using [1-¹³C]pyruvate.

Obesity is leading risk factor in the development of CVD, and is associated with an alteration in cardiac metabolism with an even greater reliance on fatty acids. Obese and lean control rodents were scanned with [1-¹³C]pyruvate, label incorporation into bicarbonate was significantly reduced in obese rats, who also displayed reduced cardiac energetics (as measured by ³¹P MRS) and diastolic function (echocardiography). These could be restored in obese rats with either 4 weeks of calorie restriction (30% reduction in calorie intake) or a week of GLP-1 agonist treatment.

We have demonstrated for the first time, that hyperpolarized MRS can detect the physiological modulation of the glucose-fatty acid (Randle) cycle in the healthy human heart. With the aim of understanding how this physiological modulation is altered in the type 2 diabetic heart and wider CVD.

