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Purpose: Dissolution-DNP together with Magnetic Resonance Spectroscopy (MRS), provides a unique tool for metabolic studies in translational animal model and in real time. We selected [1-13C]acetate (Ace), the most abundant extra- and intra-cellular short-chain fatty acid (SCFA), to clarify a fundamental pathway of the cardiac metabolism. We propose an analysis of total Areas Under the Curve (AUC) of the detected metabolites for real-time assessment of the cardiac metabolic flux and enzymatic reactions of hyperpolarized [1-13C]Ace at 3T, in a large animal model.

Methods: 4 pigs (25±2 Kg) underwent to bolus injection of hyperpolarized Na [1-13C]acetate (3 mmol, 150 mM), at rest and after administration of dobutamine (20 μg for 5 min), to increase cardiac workload. Dissolution-DNP of Na [1-13C]Ace large volumes (600 μL, [13C]=7.3 M) was set up. 13C-spectroscopic signal was acquired every 2 s for 120 s, from an axial slice selected through the heart of the pig (slice thickness = 40 mm), using a (slice-selective) pulse-and-acquire sequence (soft pulse excitation, bandwidth 2200Hz, 2048 pts, 10° flip angle). A 3T GE Excite HDxt clinical scanner (GE Healthcare, USA) and a 13C quadrature birdcage coil (Rapid Biomedical, Germany) were used for the experiments. Dynamic metabolic curves were extracted using AMARES implemented in jMRUI 3.0; fitting and AUC estimation of the metabolic curves were performed in Matlab.

Results: The spectroscopic signals of [1-13C]Ace and of its by-product [1-13C]acetyl-carnitine (AcCar) were detected in a selected slice covering the heart of the pig. We found a bimodal shape for the kinetics of [1-13C]Ace in vivo, which could be modeled using a γ-variate and a mono-exponential function (Fig.1). We recorded a significant correlation (R²=0.84, Fig.2) between the ratio of [1-13C]AcCar to [1-13C]Ace AUC and the measured Rate Pressure Product (RPP = heart rate (bpm) * systolic pressure (mmHg)).

Discussion & Conclusion: The rapid uptake and compartmentalization of [1-13C]Ace by myocardial cells was suggested by the biphasic shape of its metabolic curve; moreover the amount of produced [1-13C]AcCar quantitatively correlated with the inotropic workload of the heart. Our findings demonstrate the sensitivity of this approach in a translational large animal model, thus proving the feasibility of cardiac metabolism assessment in vivo with MRS of hyperpolarized [1-13C]Ace, with future relevance for pre-clinical and clinical studies.