Assessing overall oxidative metabolism of high-metabolic-rate abdominal organs in diet-induced obesity using compartmental modeling of [^{11}C]acetate-PET

Usevalad Ustsinau[1], Marius Ozenil[1], Antonia Grosinger[2], Thomas Wanek[1], Markus Hacker[1], Martin Kršśák[3], Cecile Philippe[1]

(1) Department of Biomedical Imaging and Image-Guided Therapy, Medical University of Vienna, Vienna, Austria
(2) Department of Health Sciences, University of Applied Sciences Campus Vienna, Vienna, Austria
(3) Department of Medicine III, Medical University of Vienna, Vienna, Austria

[^{11}C]Acetate PET imaging is a powerful tool for visualizing and studying metabolic processes in various tissues and organs, particularly in the context of heart disease and prostate cancer. The tracer can reflect tissue perfusion, oxidative metabolism, and fatty acid synthesis[1].

Male Sprague Dawley rats on standard (SD n=6) and after 8-10 weeks on a high-fat diet (HFD n=6) were studied for [^{11}C]acetate turnover. Longitudinal utilization of the tracer in the abdomen was recorded using Siemens Inveon μ-PET/CT. Under isoflurane anesthesia, rats underwent 60 min dynamic [^{11}C]acetate-PET scans and additionally on the next week venous blood sampling for [^{11}C]CO_2-metabolite analysis (7-time points; SD n=3; HFD n=3) accordingly[2]. Delineation of kidneys, myocardium, and liver; SUV calculations; 1-tissue compartmental modeling with blood-to-plasma ratio and [^{11}C]CO_2-metabolite correction were performed in PMOD3.8; clearance rate was calculated in Carimas2.1.

Semi-quantification methods demonstrated contrasting outcomes between the groups. Increased renal (right p=0.04, left p=0.03) and myocardial (p=0.01) uptake (Fig.A) was observed in the HFD group, while clearance rates in kidneys (right p=0.01, left p=0.04) and liver (p=0.03) were decreased (Fig.B). Blood sampling for [^{11}C]CO_2-metabolite analysis revealed differing profiles between the groups, with a maximum peak at 30 min in SD and two peaks at 5 and 40 min in HFD animals (Fig.C). Deeper analysis using 1-tissue compartmental modeling shed light on the hepatic uptake and showed a difference in the volume of distribution (V_t), which was significantly decreased in the HFD group ($p<0.001$) (Fig.D).

The study indicates [^{11}C]acetate accumulation in metabolically active organs: kidneys, heart, and liver. Compartmental modeling demonstrated the necessity of metabolite correction for quantitative analysis. Previously, Sprague Dawley rats on HFD were studied for fatty acid uptake and decline of VLDL synthesis[3] that can correlate with the variation of V_t in the liver and confirm pathological changes in organ functioning.

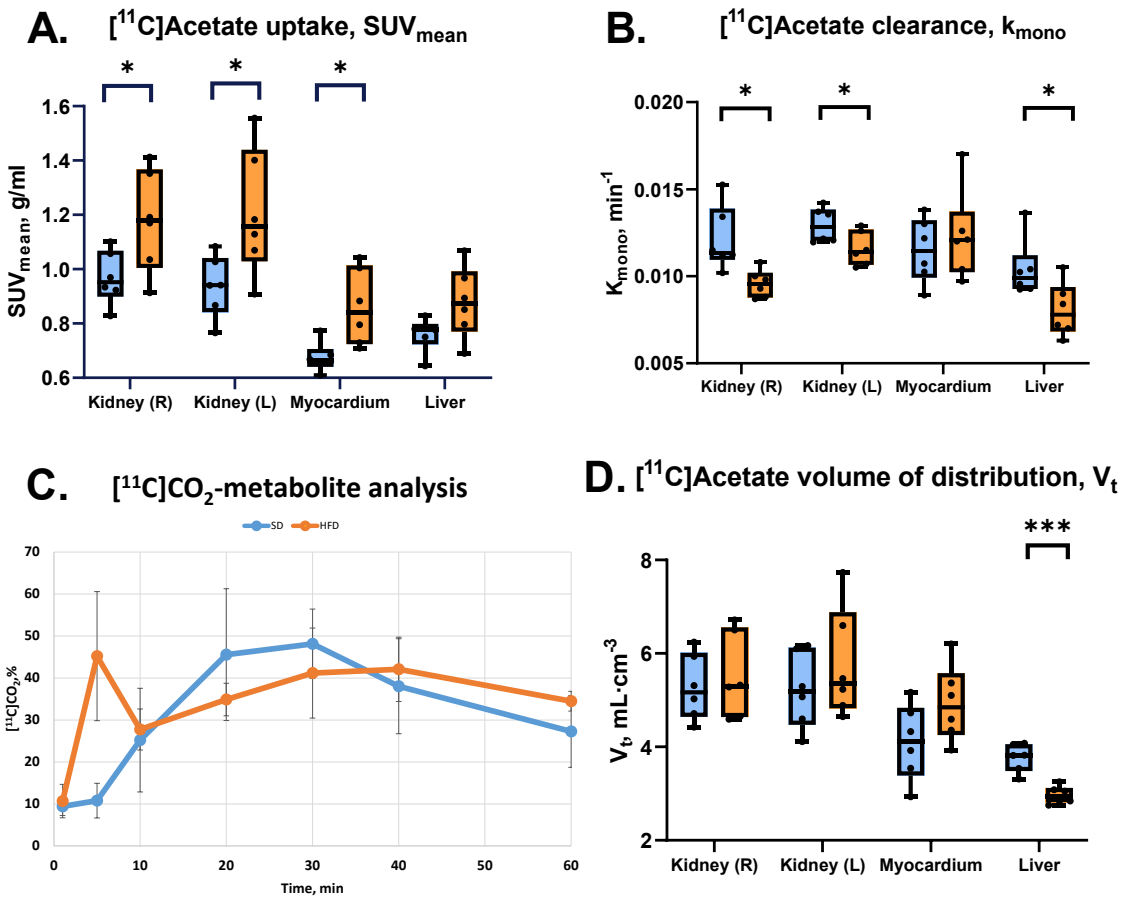

Figure. 1 Results of quantification analysis in abdominal organs and venous blood in standard diet (blue) and high-fat diet (orange) groups of rats: **A.** 60 min organ [^{11}C]acetate uptake; **B.** Mono-exponential clearance of [^{11}C]acetate; **C.** Time curves of [^{11}C]CO_2-metabolite analysis in the blood; **D.** The volume of distribution of [^{11}C]acetate. Data are mean ± SD (*p ≤ 0.05, ***p ≤ 0.001)

References:

(1) Lindhe, O., Sun, A., Ulin, J., Rahman, O., Långström, B., & Sörensen, J. (2009). *[(18)F]Fluoroacetate is not a functional analogue of [(11)C]acetate in normal physiology.* European journal of nuclear medicine and molecular imaging, **36**(9), 1453–1459. https://doi.org/10.1007/s00259-009-1128-7

(2) Ng, Y., Moberly, S. P., Mather, K. J., Brown-Proctor, C., Hutchins, G. D., & Green, M. A. (2013*). Equivalence of arterial and venous blood for [11C]CO2-metabolite analysis following intravenous administration of 1-[11C]acetate and 1-[11C]palmitate.* Nuclear medicine and biology, **40**(3), 361–365. https://doi.org/10.1016/j.nucmedbio.2012.11.011

(3) Ustsinau, U., Ehret, V., Fürnsinn, C. , Scherer, T., Helbich, T. H., Hacker, M., Kršśák, M., & Philippe, C. (2023). *Novel approach using [18F]FTHA-PET and de novo synthesized VLDL for assessment of FFA metabolism in a rat model of diet induced NAFLD.* Clinical nutrition, **42**(10), 1839–1848. https://doi.org/10.1016/j.clnu.2023.08.001