STIFTUNG FÜR LEBERKRANKHEITEN

Universitätsklinik für Viszerale Chirurgie und Medizin
Hepatologie

Non-invasive detection of metabolic liver disease

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Summary / Brief outline of topic

Overall, my PhD focuses on the non-invasive diagnosis of liver disease within a broader translational research framework. This includes several interlinked initiatives aimed at phenotyping and mechanistic elucidation of metabolic liver disease.
One key component is the DMETER project, which involves the systematic development of a comprehensive database encompassing over 1000 liver biopsy datasets, enriched with clinical, biochemical, and histological metadata. The project currently engages three master's students and one doctorate candidate, who are actively contributing to data collection and exploratory analysis.
In parallel, the CRSK3 project, conducted in collaboration with the metabolomics group, has completed all primary analyses and is in manuscript preparation.
Additionally, the FIMADIA project, focusing on screening for liver disease in individuals with diabetes type 2, has reached completion, with its corresponding manuscript currently undergoing peer review.
In this progress report, I will be focusing on the LEMON type 1 diabetes (T1D) project. The LEMON project, executed in collaboration with Prof. Lia Bally of UDEM, aimed to investigate liver-specific glucose metabolism in individuals with T1D and gastric bypass surgery using deuterium metabolic imaging combined with ^{13}C-magnetic resonance spectroscopy.
Together, these efforts provide a complementary set of tools and datasets that support biomarker identification and contribute to a better understanding of metabolic liver disease.

Activities

Clinical work: I was promoted to deputy attending in addiction medicine at Klinik Südhang in 06/2024, and appointed head of the inpatient withdrawal program in 12/2024. In this role, I currently oversee a multidisciplinary team comprising five psychologists and one medical resident, with responsibilities for around thirty patients. I have completed board certification in Internal Medicine and am preparing to take the Swiss qualification "Fähigkeitsausweis Abhängigkeitserkrankungen" in May 2025.
Teaching: I am currently supervising three master's students and one doctoral student. One master's student is expected to complete and defend his thesis in May 2025, while the others are contributing to the DMETER project, supporting data acquisition and analysis. I remain actively engaged in academic teaching, having delivered presentations at the Swiss HepCup summarizing updates from EASL and AASLD 2024, and recently led a teaching session on steatotic liver disease for medical students at the University of Bern in February 2025.
Research: The DMETER project is currently active in data collection and database expansion, aiming to include >1000 liver biopsies alongside detailed clinical and histological metadata. As a longitudinal research registry, we are in the process of developing multiple secondary analyses and publication projects. The FIMADIA project, which focused on screening strategies for metabolic liver disease in type 2 diabetes, is in the publication phase. The CRSK3 project, in collaboration with the metabolomics group, has completed data analysis and is currently being drafted into a manuscript. The LEMON RYGB study has been published, and we are now finalising the manuscript for the T1D arm of the project.

Brief Methods and results specific to LEMON T1D project

In the LEMON T1D project, we applied deuterium metabolic imaging (DMI) and interleaved ^{13}C-magnetic resonance spectroscopy (MRS) at 7 Tesla to non-invasively assess hepatic glucose and

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glycogen dynamics following oral glucose ingestion. Ten individuals with T1D and ten matched healthy controls consumed 60 g of [6,6′-$^{2}H_{2}$]-glucose. DMI was used to quantify hepatic uptake of deuterated glucose, while ^{13}C-MRS assessed glycogen content. Frequent venous blood sampling was performed to determine plasma glucose, insulin, and glucagon concentrations, and to differentiate exogenous from endogenous glucose. Glucose fluxes were modelled using the single-tracer oral minimal model, adapted to account for T1D-specific insulin dynamics, including differences in timing and formulation of exogenous insulin administration.
Compared to healthy controls, individuals with T1D exhibited impaired suppression of endogenous glucose production, prolonged hepatic D-Glc accumulation, and reduced hepatic insulin sensitivity despite higher insulin exposure. Subgroup analysis revealed distinct metabolic phenotypes within the T1D group, with differences in hepatic glucose uptake and glycogen synthesis trajectories. These findings suggest that the pattern and timing of insulin exposure, rather than total insulin levels, may play a key role in modulating hepatic glucose handling in T1D.

Discussion

These results demonstrate that postprandial hepatic glucose handling is markedly altered in T1D. The disrupted portal-to-systemic insulin gradient appears to impair insulin-mediated suppression of glucose production and modulate hepatic glucose uptake. Intra-group differences suggest heterogeneous pathophysiological mechanisms, possibly influenced by insulin timing, absorption dynamics, and intestinal glucose transit. DMI coupled with stable isotope flux analysis provides a novel, physiologically relevant approach to dissecting hepatic metabolism in T1D.

Achievements (Grants / Prizes / Publications)

CRSK3 abstract accepted for poster presentation at EASL Steatotic Liver Disease Conference 2025.
LEMON RYGB publication "In vivo mapping of postprandial hepatic glucose metabolism using dynamic magnetic resonance spectroscopy combined with stable isotope flux analysis in Roux-en-Y gastric bypass adults and non-operated controls: A case-control study" (https://pmc.ncbi.nlm.nih.gov/articles/PMC11618218/)

Outlook / Next steps

Clinical work: I plan to establish an integrated care pathway within the hepatology clinic that addresses the needs of patients with substance use disorders. This initiative aims to improve continuity of care between addiction medicine and hepatology, promoting a more holistic and patient-centred model. Key goals include improving access to addiction-specific resources, enhancing interdisciplinary collaboration, and streamlining referral processes within existing clinical infrastructure.
Teaching: I aim to further develop bidirectional teaching activities bridging addiction medicine and hepatology. This includes contributing to the 'liver gym' seminar series for hepatology fellows with a focus on managing alcohol use disorder, as well as integrating structured teaching sessions on liver disease into the clinical education program at the addiction medicine clinic. These sessions target residents and psychologists working with patients who present with both liver pathology and substance use disorders, aiming to promote interdisciplinary understanding and care integration.
Research: Over the next months, I aim to complete and submit my PhD thesis. This includes the finalisation and submission of manuscripts from the CRSK3, FIMADIA, and LEMON T1D projects, which are each at an advanced stage of preparation. I am also preparing a first manuscript based on the DMETER registry, focusing on sex-specific performance of non-invasive diagnostic markers for liver fibrosis. Additional DMETER-based subprojects are currently being planned and developed in parallel.