Development of deuterium metabolic imaging to map body biochemistry with MRI

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Primary objective: Develop a completely novel and non-invasive method to map body metabolism in humans based on DMI on a 7T MRI scanner.Secondary objectives: To demonstrate proof of concept by measuring (1) hepatic glucose metabolism and (2) de...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Observational invasive

Summary

ID

NL-OMON56442

Source
ToetsingOnline

Brief title
BodyDMI

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Diabetes mellitus type 2, type 2 diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: NWO TTW

Intervention

Keyword: Diabetes, Liver, Metabolic imaging, MRI

Outcome measures

Primary outcome

The main study parameters are 3D DMI measurements of hepatic carbohydrate and lipid metabolism in the liver of healthy volunteers and type 2 diabetes patients. Specifically we will determine rates of glucose uptake and metabolism (study 1) and the fraction of de novo synthesized lipids in the liver lipid pool (study 2).

Secondary outcome

Not applicable

Study description

Background summary

In type 2 diabetes, both carbohydrate and lipid metabolism in the liver are dysregulated, which is strongly related with hepatic insulin resistance. However, our knowledge of the exact disturbances in the metabolic pathways in the insulin resistant liver is limited due to the fact that sensitive, direct measurement methods are currently lacking. The aim of this project is to develop a completely novel and non-invasive method to measure hepatic carbohydrate and lipid metabolism directly inside the liver in humans. The method is based on deuterium metabolic imaging (DMI) combined with administration of deuterated compounds. We expect that DMI has sufficient sensitivity to dynamically probe metabolic pathways in the human liver in 3D imaging mode.

Study objective

Primary objective: Develop a completely novel and non-invasive method to map body metabolism in humans based on DMI on a 7T MRI scanner.
Secondary objectives: To demonstrate proof of concept by measuring (1) hepatic glucose metabolism and (2) de novo

lipogenesis in the liver using DMI, in healthy volunteers and patients with type 2 diabetes.

Study design

Two feasibility studies will be carried out to measure (1) hepatic glucose metabolism and (2) de novo lipogenesis in the
liver using DMI, in healthy volunteers and patients with type 2 diabetes.

Study burden and risks

Subjects participating in study 1 will visit the UMC Utrecht once. After an overnight fast, subjects will get an MRI scan which takes approximately 120 min. Before or during the scan, they will receive an oral dose of deuterated glucose (maximum 0.75 g/kg body weight) dissolved in water. The glucose solution can be consumed slowly (in 5-10 min).To avoid multiple vena punctures and to be able to collect blood samples during the MRI, an intravenous access site will be installed in a vein in the arm to collect blood samples. A blood sample of 20 ml will be collected before the oral glucose dose, and 12 small blood samples of 3 ml will be collected during the 120 min after the oral glucose dose.
Subjects participating in study 2 will visit the UMC Utrecht twice. On day 1, subjects will undergo a baseline 7T MRI scan at the 7T MRI scanner (in the fed state), which will take approximately 60 min. After the scan, volunteers will receive an initial bolus of heavy water of 3.5 ml/kg body water. From day 2 until day 5, volunteers will consume a maintenance dose of heavy water of 1.25 ml/kg body water. On day 5, subjects will get another 7T MRI scan, which will take approximately 60 min. Blood samples of 20 ml will be collected on day 1 before the bolus administration of heavy water, and on day 5 before the MRI scan.
The intake of above mentioned amounts of deuterated glucose and heavy water, and drawing of the above mentioned amount of blood does not affect the health of participants. Deuterium (2H) is a stable, non-radioactive, isotope of hydrogen, and biologically, deuterated glucose and heavy water behave similarly to normal glucose and normal water, respectively. No adverse effects have been observed with oral administration of deuterated glucose at the dosage which will be used in this study. When body water deuterium enrichment reaches 3%, subjects can experience dizziness and/or nausea, because it affects the density of the fluid in the inner ear, but this effect is only temporary (disappears within a few hours) and no long-term adverse effects have been reported. The bolus of heavy water will therefore be consumed in small portions during the day and this will take place in the UMC Utrecht under supervision of medical staff. MRI is a safe and reliable technique for subjects without contra-indications for undergoing MRI and is widely used in clinical examinations and scientific research. Subjects included in the study will have no contra-indications for MRI and they will be screened again for

contra-indications before undergoing the MRI examination(s). To ensure technical feasibility, the MRI protocol will behas been extensively pilot-tested in healthy subjects at natural abundance according to METC-protocol number 15-466, showing good sensitivity and stability of the 3D DMI measurements.
To our knowledge, there is no risk of participation in this study other than the small risk associated with venipuncture.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

All subjects:
• Age > 40 and younger than 70 years (healthy controls and type 2 diabetes patients matched for age; age differences of ± 5 years will be allowed)
• Sex: male

• Ability and willing to give informed consent
• Ability to follow test instructions
• Sufficient understanding of the Dutch language

Healthy control subjects:
• BMI: 20-25 kg/m2

Type 2 diabetes patients:
• Patients diagnosed with type 2 diabetes for at least 1 years
• BMI: 20-35 kg/m2

Exclusion criteria

All subjects:
• Contra-indications to MRI examination according to 7T MRI screening guideline of the UMC Utrecht
• An average alcohol consumption of >21 standard drinks per week
• Abnormal liver function (fibrosis)

Type 2 diabetes patients:
• Use of exogenous insulin
• Known causes of hepatic steatosis other than non-alcoholic fatty liver disease

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-04-2023

Enrollment:	40
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	28-04-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	15-11-2023
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL76275.041.21