# DiabetEs Type 2 and thE Role of MacroalbumInuria; a diagnostic tool for vascular ageing with 18F-NaF PET/CT imaging

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Primary Objective:To investigate whether arterial microcalcification (18F-NaF-PET detected) and macrocalcification (CT detected) are increased in patients with T2D who have macroalbuminuria as compared to patients with normoalbuminuria.Secondary...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Diabetic complications
Study type	Observational invasive

## Summary

### ID

NL-OMON50619

**Source** ToetsingOnline

Brief title DETERMINE

## Condition

- Diabetic complications
- Nephropathies
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

#### Synonym

atherosclerose, vascular stiffness

#### **Research involving**

Human

## **Sponsors and support**

**Primary sponsor:** Universitair Medisch Centrum Groningen **Source(s) of monetary or material Support:** Siemens Healthcare

#### Intervention

**Keyword:** Adipose tissue volume, Diabetes, Macroalbuminuria, NaF PET/CT imaging, Pulse wave velocity

#### **Outcome measures**

#### **Primary outcome**

Vascular 18F-NaF uptake (proxy for vascular macrocalcification) is quantified

by using target-to-background ratios (TBRs).

#### Secondary outcome

\* CT assessed arterial macrocalcification using measurement of hounds field

units.

- \* Albuminuria assessed in 2 separate 24-hours urine samples
- \* Carotid-femoral PWV assessed arterial stiffness
- \* C-reactive protein (CRP) assessed systemic inflammation
- \* VAT volume assessed with CT
- \* SAT volume assessed with CT
- \* Body weight, length, BMI
- \* Adipokines: adiponectin and leptin
- \* Glycemic indices: HbA1c, insulin, HOMA-IR, fasting glucose
- \* Lipid parameters: total cholesterol, LDL-cholesterol, HDL-cholesterol,
- triglycerides, apo-B, PCSK9 levels
- \* Systolic and diastolic blood pressure
- \* Kidney function and degree of albuminuria assessed using 24-hours urine
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creatinine clearance and albumin-to-creatinine ratio (ACR)

\* Plasma calcium phosphate metabolism plasma markers, including calcium,

albumin, phosphate, vitamin D3, fetuin A, klotho, fibroblast growth factor 23,

parathormone, serum calcification propensity score (T50).

## **Study description**

#### **Background summary**

Type 2 diabetes mellitus (T2D) is associated with a strong increase in cardiovascular risk, which is a consequence of accelerated vascular ageing. This process is hallmarked by vascular remodeling, chronic low-grade inflammation, calcification, and increased vascular stiffness. Expected is that vascular ageing is more pronounced in T2D patients who are also suffering from macroalbuminuria. In particular T2D patients are accompanied with obesity, and whereas visceral adipose tissue (VAT) is playing a central role in causing insulin resistance and metabolic syndrome. VAT is distributed through the abdominal cavity and is present surrounding the abdominal organs and the vasculature.

To study whether vascular calcification in T2D subjects with or without macroalbuminuria is more prominent, the whole body, and therefore vasculature, will be imaged with 18F-NaF PET. With this nuclear tracer, microcalcification and therefore vascular ageing, will be imaged. The intensity of vascular calcification on PET will be compared with CT assessed macrocalcification and vascular ageing markers such as vascular stiffness and calcium phosphate metabolism. Besides that, the role of adipose tissue will be studied. Adipose tissue volumes of VAT and subcutaneous adipose tissue (SAT) will be ranked and compared to vascular calcification. This clinical project will supply insight information of the additional risk of macroalbuminuria in the accelerated vascular ageing of T2D patients.

#### Study objective

Primary Objective:

To investigate whether arterial microcalcification (18F-NaF-PET detected) and macrocalcification (CT detected) are increased in patients with T2D who have macroalbuminuria as compared to patients with normoalbuminuria.

#### Secondary Objectives:

1. To investigate whether arterial microcalcification (18F-NaF-PET detected)

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and macrocalcification (CT detected) are associated with vascular stiffness (assessed by PWV).

2. To investigate whether arterial microcalcification (18F-NaF-PET detected) and macrocalcification (CT detected) are associated with components of the metabolic syndrome, including adipose tissue volumes (visceral and subcutaneous), adipokines, insulin resistance index (HOMA-IR), and HbA1c, fasting glucose, lipid metabolism, and blood pressure.

3. To investigate whether arterial microcalcification (18F-NaF-PET detected) and macrocalcification (CT detected) are associated with markers of calcium phosphate metabolism

4. To investigate which of the above mentioned factors (i.e. macroalbuminuria, metabolic syndrome, calcium phosphate metabolism, and kidney function) are independent determinants of arterial microcalcification (18F-NaF-PET detected) and macrocalcification (CT detected).

### Study design

Single center, cross-sectional, observational, case-control study in het UMCG

#### Study burden and risks

Small, slight radiationload and bruising of venapuncture.

## Contacts

#### **Public** Universitair Medisch Centrum Groningen

Hanzeplein 1 Groningen 9700RB NL **Scientific** Universitair Medisch Centrum Groningen

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## **Trial sites**

## **Listed location countries**

Netherlands

## **Eligibility criteria**

#### Age

Adults (18-64 years) Elderly (65 years and older)

### **Inclusion criteria**

Inclusion criteria T2D patients:

- \* Men and women, age above 18 years
- \* Written informed consent
- \* Using RAAS inhibitors
- \* Fulfils ADA criteria for diabetes
- o Fasting plasma glucose \* 7.0 mmol/l OR
- o Random plasma glucose \* 11.1 mmol/l OR
- o HbA1C \* 6,5%, Inclusion criteria healthy controls:
- \* Men and women, age above 18 years
- \* Written informed consent
- \* eGFR above 60 ml/min/175m2 (CKD-EPI formula)

### **Exclusion criteria**

Exclusion criteria T2D patients:

- \* Type 1 diabetes
- \* Clinically significant liver disease
- \* Other causes for macroalbuminuria than nephropathy
- \* Previous cardiovascular disease, defined as stable coronary artery disease or acute coronary syndrome, stroke or transient ischemic attack, peripheral artery disease

\* Patients who are mentally incompetent and cannot sign a Patient Informed Consent

- \* Claustrophobia
- \* Pregnancy or breastfeeding women.
- \* Current active bone malignancy or in the previous 6 months
- \* Disorders affecting bone metabolism, e.g. hyperparathyroidism, Paget's disease
- \* Systolic blood pressure > 200 mmHg,

Exclusion criteria healthy controls:

\* Type 1 or 2 diabetes

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- \* Micro- or macroalbuminuria
- \* Clinically significant liver disease
- \* Previous cardiovascular disease, defined as stable coronary artery disease or acute coronary syndrome, stroke or transient ischemic attack, peripheral artery disease
- \* Patients who are mentally incompetent and cannot sign a Patient Informed Consent
- \* Claustrophobia
- \* Pregnancy or breastfeeding women.
- \* Current active bone malignancy or in the previous 6 months
- \* Disorders affecting bone metabolism, e.g. hyperparathyroidism, Paget's disease
- \* Systolic blood pressure > 200 mmHg

## Study design

### Design

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

### Recruitment

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NL	
Recruitment status:	Recruitment stopped
Start date (anticipated):	09-01-2019
Enrollment:	50
Туре:	Actual

### Medical products/devices used

Product type:	Medicine
Brand name:	18 Fluor Sodium fluoride
Generic name:	18 Fluor Sodium fluoride
Registration:	Yes - NL intended use

## **Ethics review**

Approved WMO	
Date:	19-12-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	
Date:	05-04-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	
Date:	27-01-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

## **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
EudraCT	EUCTR2018-002347-28-NL
ССМО	NL66049.042.18