# Calibration of extracellulair fluid volume measurement by 125I-iothalamate in subjects with a low GFR using Bromide distribution volume.

Published: 06-02-2014
Last updated: 23-04-2024

Primary Objective: To calibrate the measurement of ECFV by 125I-iothalamate in subjects with a GFR

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Will not start |
| **Health condition type** | Renal disorders (excl nephropathies) |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON38842

**Source**
ToetsingOnline

**Brief title**
ECV-measurement by 125I-iothalamate in low GFR.

### Condition

- Renal disorders (excl nephropathies)

**Synonym**
chronic kidney disease stadium III and IV; diminished renal function

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Universitair Medisch Centrum Groningen
**Source(s) of monetary or material Support:** Roche Nederland BV

## Intervention

**Keyword:** 125I-iothalamate, bio-impedance, ECV-measurement, low GFR

## Outcome measures

### Primary outcome

The aim of this calibration study is the development of an empirical algorithm for calculation of the ECFV using VdIOT, that includes correction for the systematic error due to extrarenal clearance of 125I-iothalamate. To this purpose, the main study parameter is correlation of the distribution volumes of of 125I-iothalamate and Bromide in subjects with a GFR <60 ml/min, expressed in a calculated correction factor for extrarenal clearance of 125I-iothalamate.

### Secondary outcome

• Urinary clearance of 125I-iothalamate within 24 and 48 hours after administration in subjects with a GFR < 30 ml/min.

• Urinary clearance of 125I-iothalamate within 24 and 48 hours after administration in subjects with a GFR of 30-60 ml/min

• Extrarenal clearance of 125I-iothalamate in subjects with a GFR < 30 ml/min

• Extrarenal clearance of 125I-iothalamate in subjects with a GFR of 30-60 ml/min

• Difference in urinary clearance of 125I-iothalamate within 24 and 48 hours after administration in subjects with a GFR < 30 ml/min and subjects with a GFR of 30-60 ml/min.

• Difference in extrarenal clearance of 125I-iothalamate in subjects with a GFR < 30 ml/min and subjects with a GFR of 30-60 ml/min.

• Correlation of ECFV measured by bio-impedance measurements using a Maltron

Bioscan 916 to VdBromide.

# Study description

### Background summary

Extra celullar fluid volume (ECFV) is an important parameter of renal function. ECFV not only has an important role in normalisation of glomerular filtration rate (GFR) (1), but is also an important marker of renal function itself, because of the central role of the kidney in regulation of fluid balance. In previous research the feasibility of measuring ECFV during regular renal function tests using 125I-iothalamate and 131-Hippuran by distribution volume of iothalamate (VdIOT) has been tested. (2,3) The required steady state of iothalamate was reached, and a change in fluid balance induced by high sodium intake was adequately detected by a corresponding rise in the distribution volume of iothalamate (VdIOT). Therefore, VdIOT appears to be a feasible measure of the ECFV. Two factors that influence the measurement of ECFV by VdIOT are voiding errors and the extrarenal clearance of iothalamate. The latter seems to be dependent of GFR, with a higher percentage of extrarenal clearance in subjects with a lower GFR. (4) Correction for these factors can be made by collecting a recovery urine of 24 hours after iothalamate infusion. This method includes the assumption that al infused 125I-iothalamate is cleared and excreted in the urine within these 24 hours. In subjects with a low GFR this might not be true. In the aforementioned study the mean GFR was 79 ml/min and only a few subjects with a GFR <30 ml/min were included. Therefore, the validation of VdIOT as an indicator of ECFV cannot be generalised to the population with diminished renal function. Especially in this population the possibility of calculating ECFV and normalising GFR to ECFV is very useful, as it provides insights in fluid balance and pathophysiology in patients with chronic renal disease. We therefore want to calibrate VdIOT as a measure of ECFV in this population, using an accepted measurement of ECFV: distribution volume of Bromide.

### Study objective

Primary Objective:

To calibrate the measurement of ECFV by 125I-iothalamate in subjects with a GFR <60 ml/min and GFR <30 ml/min, using an accepted measurement of ECFV: distribution volume of Bromide.

Secondary Objective(s):

To determine if urinary clearance of 125I-iothalamate is complete within 48

hours in subjects with a GFR < 60 ml/min.
To determine the percentage of extrarenal clearance in subjects of 125I-iothalamate with a GFR < 60 ml/min and < 30 ml/min.

**Study design**

To be able to draw an accurate conclusion to answer our research question, the study population of this observational study will consist of 25 renal transplant recipients with a GFR of 30-60 ml/min and of 25 renal transplant recipients with a GFR <30 ml/min. This sample size is comparable to the largest validation study on this subject in the current literature. 50 adult renal transplant recipients undergoing GFR-measurement by 125I-iothalamate and 131I-Hippuran during regular post-transplant follow-up will receive an oral dose of sodium bromide in a dosage of 50 mg Br/kg. Standard blood drawings will be performed (t=0, t=90 min, 150 min, 210 min, 270 min and 330 min) and at each time point an extra 3cc of blood will be drawn for measurement of serum bromide. This serum will be centrifuged and frozen until measurement of bromide concentration at the end of the study period. At the standard time points serum concentration of 125I-iothalamate will also be measured. Subjects will be asked to collect urine from the end of the GFR-measurements up to 48 hours (2 x 24 hour samples) afterwards. This will be used for optimal calculation of the distribution volume of 125I-iothalamate.

Calculation of the extracellular volume will be done using the following equations:

For the distribution volume of Bromide (VdBromide):

$$VdBromide = \frac{Br\ dose}{[Br]before - [Br]after} \times 0.90 \times 0.95 \times 0.94$$

In this equation 0.90 is the correction factor for distribution of Bromide in non extracellular space (mainly erythrocytes), 0.95 represents the correction factor for the Gibbs-Donnan equilibrium (the high plasma content of negatively charged proteins leads to a lower concentration of negatively charged Bromide in plasma relative to the rest of the ECFV) and 0.94 the correction factor for the water concentration in serum.

For the distribution volume of 125I-iothalamate:

$$VdIOT = \frac{[IOT]\ bolus * Volume + [IOT]\ infusion\ fluid * Volume - SUM([IOT]\ urine * Volume)}{}$$

---
---
[IOT] serum in steady state

**Study burden and risks**

This study involves administration of a single, low dose of Bromide. No (serious) side effects are expected. The burden for subjects participating in this study consists of taking a single oral dose of sodium bromide (50mg/kg body weight), collection of a 48-hour urine sample and drawing and extra 18cc of blood (6x3cc). During renal function measurement, a bio-impedance measurement will be performed. This measurement takes fifteen minutes, is painless and without any risks.

# Contacts

**Public**
Universitair Medisch Centrum Groningen

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

Hanzeplein 1
Groningen 9700RB
NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

### Inclusion criteria

Undergoing renal function measurement with 125I-iothalamate during regular post transplant follow-up
>= 1 year post-transplantation
Age >=18 years
GFR 30-60 ml/min for 25/50 subjects, for 25/50 subjects GFR <30 ml/min
Informed consent

### Exclusion criteria

No understanding of the patient information
No informed consent
Underlying malignancy or infectious disease;For bio-impedance measurements:
• Pacemaker or implantable cardioverter defibrillator (ICD) making bio-impedance measurements unreliable

## Study design

### Design

**Study type:** Observational invasive

| | |
|---|---|
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Diagnostic |

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Will not start |
| Enrollment: | 50 |
| Type: | Anticipated |

## Ethics review

Approved WMO

| | |
|---|---|
| Date: | 06-02-2014 |

| | |
|---|---|
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 20-03-2015 |
| 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 |
|---|---|
| CCMO | NL42884.042.13 |