# 99mTc-mebrofenin Hepatobiliary Scintigraphy (99mTc-HBS) liver function stress test.

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| **Ethical review** | Not approved |
| **Status** | Will not start |
| **Health condition type** | Hepatobiliary neoplasms malignant and unspecified |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON41103

**Source**
ToetsingOnline

**Brief title**
**CHOCOLATE STRESS TEST**

### Condition

- Hepatobiliary neoplasms malignant and unspecified

**Synonym**
lier failure, liver insufficiency

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum
**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** Hepatobiliary Scintigraphy, ''hepatocyte reserve capacity□□, liver function, postoperative liver failure

## Outcome measures

### Primary outcome

The main objective of this study is to explore if hepatocytes have a functional

reserve capacity:

- Does oral food challenge potentiate hepatic function measured with

99mTc-mebrofenin HBS?

### Secondary outcome

The secondary objective of this study is to explore if patient*s age influences

the liver function and the hepatic reserve capacity:

- Does initial liver function measured with 99mTc-mebrofenin HBS differ between

young and elderly patients?

- Does liver function after oral food challenge measured with 99mTc-mebrofenin

HBS differ between young and elderly patients?

# Study description

### Background summary

Surgical resection remains the only potentially curative treatment option for patients diagnosed with primary or metastatic hepatic tumor. Liver resection, when performed in the absence of sufficient FRL function inevitably leads to post-resectional liver failure (PLF), a severe and potentially life threatening complication.

Computed tomography (CT) volumetry is considered the gold standard in the preoperative assessment of patients scheduled for major liver resection. Though, FRL volume does not necessarily reflect liver function. 99mTc-mebrofenin hepatobiliary scintigraphy (HBS) is a validated quantitative liver function test and in being used in the AMC for the preoperative assessment of patients scheduled for major liver resection and patients who undergo portal vein embolization.

Currently we use one single cut off value (2.69%/min/m2) for HBS in order to decide if the measured liver function is sufficient for a patient to undergo hepatic resection. Though, HBS is performed after 4 hours fast which could mean that the liver function measured is the **rest liver function** in stead of **maximum function** of the FRL.

We hypothesize that some patients have a great **reserve capacity**. This information could be of crucial importance in the preoperative patient selection process especially in patients considered *borderline* operable due to their low liver function. Furthermore, we do expect young patients to differ in their **hepatocyte reserve capacity** compared to elderly patients.

## Study objective

In this study we will explore changes in the hepatic function after stimulation of hepatic cells with an oral food challenge, the **hepatocyte reserve capacity**. Moreover, we will explore potential differences in the hepatocyte reserve capacity between young (25-45 years) and elderly (*75 years) subjects.

In case of encouraging study results, the study will be continued in patients who will undergo a hepatic resection.

## Study design

This study is designed as a prospective observational pilot study in 24 healthy subjects.

## Study burden and risks

Radiation burden for the participants increases as a consequence of HBS, which we want to reduce as much as possible. For this reason, HBS will be performed without SPECT-CT, which is normally performed together with 99mTc-mebrofnine-HBS. This is possible because information that is obtained by SPECT-CT is not relevant for our endpoints. In case of patients who undergo HBS prior to liver resection of portal vein embolization, SPECT-CT is an essential part of liver function measurement. This adjustment reduces the radiation burden for the participants with 50%. Furthermore, we will reduce the dose with another 50% by performing HBS with 100 MBq 99mTc-mebrofenin instead of 200 MBq

(200 MBq is the clinical routine for HBS-SPECT-CT). This reduction is also possible due to the fact that HBS will be performed without SPECT-CT. The total radiation burden for the participants in this study will be 3.4 mSv for both scans (instead of 13.6mSv for both scans in case of routine HBS with SPECT-CT). As already mentioned, this dose is in category IIb of ICRP (report ICRP62), qualified as an intermediate risk. We will advise the subjects not to participate in this kind of studies more often than once per 4 years. There are no known complications related to HBS.

For this study we will include healthy volunteers. In order to insure reliable measurements, we need to include healthy participants without underlying parenchymal diseases. In this light, we are not able to include patients who will undergo HBS as part of their clinical assessment. Liver malignancies are often accompanied by parenchymal diseases such as cirrhosis, fibrosis or cholestasis. Moreover, this patient population is often treated with neoadjuvant chemotherapy which has a great impact on liver function.

Participants need to fast overnight prior to each scan, which is burdensome for the subjects. Though, patients who undergo HBS as standard preoperative assessment or because of portal vein embolization experience little discomfort due to the fasting. HBS will be scheduled the next morning. For each scan, participants will not need to fast longer than 4 hours during the day (4 hour fast is the routine for patients who undergo HBS in the clinical setting). The total time investment will be maximal 9 hours. Travel expenses for the extra visits to the hospital will be reimbursed.

An i.v. canula will be placed prior to each HBS scan. In this way we are able to reduce the burden as using the i.v. canula 1) we will draw blood in order to obtain biochemical parameters and 2) subjects will be injected with 100 MBq 99mTc-mebrofenin.

Standard clinical assessment will be performed prior to the first HBS-scan which will be done by means of a number of questions aimed at participant*s medical history and current health status. These questions are necessary in order to ensure our exclusion criteria.

The counterpart of the burden is the possible impact of this study on our future preoperative patient selection. Each day we see patients who are considered *borderline* operable due to their low FRL function. This is a difficult situation for every patients as we need to decide between 1) performing liver resection with a realistic chance on developing postoperative liver failure, which has a mortality risk of 80% or 2) no resection, though liver resection is the only potentially curative option. In our opinion, the social benefits that can be achieved with this study should not be neglected.

In case of encouraging study results, the study will be prospectively continued

in patients who will undergo a hepatic resection.

## Contacts

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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

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

### Inclusion criteria

Healthy volunteers.
Age 25-45 or *75 years.
Signed informed consent obtained prior to any study-specific procedure

### Exclusion criteria

Age <25 years or between 46-74 years.

Known with hepatic disease (e.g. cirrhosis, steatosis, cholestasis, hepatitis).
Underwent hepatic procedures in the past (e.g. portal vein embolization, radio frequent ablation, hepatic resection).
Treated with chemotherapy in the past.
Allergies/intolerance for the challenge agent (e.g. lactose or any other ingredients of the chocolate-milk).
Pregnancy or breastfeeding.
Not able to sign informed consent.

# Study design

## Design

**Study type:** Observational invasive

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

## Recruitment

NL

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|---|---|
| Recruitment status: | Will not start |
| Enrollment: | 24 |
| Type: | Anticipated |

# Ethics review

Not approved

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| Date: | 15-12-2014 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |

# 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 | NL50147.018.14 |