# Early detection of breast cancer using markers in nipple aspirate fluid, blood, and tumor material from women with breast cancer compared to healthy women.

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Circulating miRNAs can be easily measured in body fluids which, in case of nipple fluid, could offer a promising minimally invasive method to complement current breast cancer screening methods, especially for high-risk women. In this study we aim to...

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Breast neoplasms malignant and unspecified (incl nipple) |
| **Study type** | Observational non invasive |

## Summary

### ID

NL-OMON28422

**Source**
Nationaal Trial Register

**Brief title**
ORNAMENT

### Condition

- Breast neoplasms malignant and unspecified (incl nipple)

**Health condition**

Mamma carcinoma, breast cancer, biomarkers, screening

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** University Medical Center Utrecht
**Source(s) of monetary or material Support:** Stichting Vrienden UMC Utrecht

## Intervention

- Other intervention

**Explanation**

## Outcome measures

**Primary outcome**

To assess the microRNA expression levels in nipple aspiration fluid obtained just before primary surgery. These will be compared to the microRNA expression levels in NAF obtained from healthy controls (which is already available at our department; study NL41845.041.12).

**Secondary outcome**

Within patients, to compare microRNA expression in nipple aspiration fluid from the cancerous breast to microRNA expression in:

1. tumor material obtained at surgery

2. blood

3. NAF from the contralateral breast

# Study description

**Background summary**

We previously showed that we can successfully obtain nipple fluid by aspiration and assess microRNA expression levels isolated from this fluid. For further validation of the clinical value of this potential novel screening method, it is crucial to determine how well microRNA expression patterns discriminate NAF derived from cancerous and healthy breasts. Therefore, we will preoperatively aspirate nipple fluid from women having just been diagnosed with or suspected of breast cancer, and compare microRNA expression patterns in nipple fluid derived from cancerous breasts, contralateral unaffected breasts, and healthy controls. In addition we will determine microRNA expression levels in the tumor and blood of the breast cancer patient. Our ultimate goal is, through monitoring of biomarkers in nipple fluid, to develop a reliable method that on one hand allows postponing or avoiding mutilating

prophylactic breast surgery as much as possible (reducing morbidity) while on the other hand determining the right time to intervene, thereby preventing development of invasive breast cancer (reducing mortality).

**Study objective**

Circulating miRNAs can be easily measured in body fluids which, in case of nipple fluid, could offer a promising minimally invasive method to complement current breast cancer screening methods, especially for high-risk women. In this study we aim to assess the microRNA expression levels in nipple aspiration fluids of women with recently diagnosed breast cancer where we will compare the results to those obtained in healthy controls (which is already available at our department; study NL41845.041.12). The ultimate goal is to more accurately predict the onset of breast cancer.

**Study design**

Multicenter cross-sectional observational study

**Intervention**

In this monocenter, cross-sectional study, nipple aspiration will be performed preoperatively in women that are recently diagnosed with, or are suspected to have breast cancer.

Nipple fluid collection:

Nipple fluid will be collected by qualified and trained study UMC Utrecht personnel at the UMC Utrecht.

This will be done before surgery in patients with biopsy proven invasive breast cancer, or in BIRADS 4/5 patients by mammography before taking the core needle biopsy for histological diagnosis.

In short:

1) The subjects are given one spray (4 IE) of oxytocin in both nostrils;

2) The nipple is gently wiped with Nuprep Skin Prep Gel in order to remove keratin plugs and subsequently cleansed with ethanol (see separate attachment);

3) Nipple fluid will be obtained by means of a manual device: A suction cup (aspirator) is placed over the nipple. Repeated gentle suction by a syringe (10-20 cc) draws fluid from inside the duct to the nipple surface. Fluid droplets are collected by capillary tubes. The entire procedure is repeated at the other breast.

Drawing blood

Three vials of blood will be drawn. This is not a mandatory part of the study and the patients will be asked for separate consent.

**Study burden and risks**

An earlier study showed that the burden associated with nipple fluid aspiration is minimal and the procedure is well tolerated. To further minimalize any discomfort, nipple fluid will as much as possible be collected at the time of regular visits to the hospital or outpatient clinic. The risks of the procedure are negligible.

However, a few steps within our protocol could potentially lead to side effects, consisting of:

Oxytocin nasal spray: painful contraction of the uterus (sometimes; 0.1-1%); headache, nausea, vomiting, allergic skin reaction (rarely; 0.01-0.1%).

Nipple numbing cream: redness, skin discoloration, skin thickening at site of application (often; 1-10%); warm, sensitive, burning, itching feeling of the skin (sometimes; 0.1-1%)

Nipple fluid aspiration: sensitive or painful breasts, skin irritation, redness of bruising (mild/seldom)

Blood collection: bruising; lightheadedness; fainting, infection at the site where the needle was inserted into the skin

# Contacts

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# Eligibility criteria

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

## Inclusion criteria

- Female age ¡Ý18 years

- Signed informed consent

- Proven invasive breast carcinoma; or suspected invasive breast cancer (BIRADS 4 or 5)

- Willing and able to comply to the study protocol

## Exclusion criteria

- Bilateral breast reduction with nipple graft

- Bilateral ablative breast surgery

- Pregnancy or lactation

- Active breast infection

- Disseminated breast cancer

# Study design

## Design

| | |
|---|---|
| Study phase: | N/A |
| Study type: | Observational non invasive |
| Intervention model: | Single |
| Allocation: | Non controlled trial |
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Screening |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 01-01-2017 |
| Enrollment: | 137 |
| Type: | Actual |

## IPD sharing statement

**Plan to share IPD:** No

# Ethics review

Approved WMO

| | |
|---|---|
| Date: | 12-12-2016 |
| Application type: | First submission |
| Review commission: | METC NedMec |

# Study registrations

## Followed up by the following (possibly more current) registration

ID: 50271
Bron: ToetsingOnline
Titel:

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

No registrations found.

## In other registers

| Register | ID |
|---|---|
| NTR-new | NL6031 |
| NTR-old | NTR6162 |
| CCMO | NL57343.041.16 |
| OMON | NL-OMON50271 |

# Study results