# Onderzoek naar het bepalen van de reactie op chemotherapie van tumorcellen in de borst en in de oksel.

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| **Ethische beoordeling** | Positief advies |
| **Status** | Werving gestart |
| **Type aandoening** | - |
| **Onderzoekstype** | Interventie onderzoek |

## Samenvatting

### ID

NL-OMON21498

**Bron**
Nationaal Trial Register

**Verkorte titel**
N08RMB

**Aandoening**

breast cancer
neoadjuvant chemotherapy
axillary lymph node metastasis
FDG-PET/CT
Iodine-125 seeds

### Ondersteuning

**Primaire sponsor:** Philips
**Overige ondersteuning:** CTMN project

### Onderzoeksproduct en/of interventie

## Uitkomstmaten

### Primaire uitkomstmaten

Sensitivity and specificity of FDG PET and MRI to predict a favourable tumour response of the primary tumor defined as (near) pathological complete remission
Sensitivity and specificity of FDG PET/CT and radioactive I-125 seed localisation to predict a favourable tumour response of the axilla, defined as pathological complete remission or residual micrometastasis.

# Toelichting onderzoek

### Achtergrond van het onderzoek

1. Response monitoring of the primary tumor:

We will weigh the value of FDG-PET imaging against dynamic contrast-enhanced MRI to evaluate response of the primary tumor. It is expected that these modalities will complement one another in two ways:
A. MRI provides information on perfusion, whereas FDG provides tumor information on cell metabolism;

B. FDG PET may provide earlier assessment of tumor response than MRI for subgroups of patients.

In order to establish the optimal time point for FDG PET we will perform the PET early after initiating treatment and together with MRI at a later stage during treatment. The PET will be performed in prone orientation of the patient using a support system identical to the breast coil used at MRI. MRI and PET will be registered. Changes in the maximum standardized uptake
value (SUV) in the tumor and changes in size will be established at PET. At MRI changes in size of initial contrast uptake, and washout will be established. Presence/absence of residual disease at histopathology will be used as a surrogate end-point of tumor response. A favorable response is defined as a pathological complete remission (pCR); no residual tumor cells seen at microscopy, or a near pCR; a small number of scattered tumor cells. Multivariate analysis of changes in FDG uptake and MRI contrast uptake will be employed to establish quantitative guidelines to discriminate between favourable and non-favourable responders during neoadjuvant therapy. The guidelines will be constructed in a training set of cases and prospectively applied in a validation set of cases.

2. Response monitoring of the axilla:

In the group of cN1 patients, axillary tumor response will be evaluated using two different methods.

A. FDG-PET/CT. Patients will receive three FDG-PET/CT. One scan prior to primary systemic therapy, two PET scans during systemic therapy. ALND will be performed in all patients. The axillary tumor response as seen on FDG-PET will be compared with pathological assessment of the lymph nodes after ALND;

B. Radioactive seed localization (RSL). The tumor positive axillary lymph node will be marked prior to primary systemic therapy. In the same session of surgery for the breast tumor after systemic therapy, the marked lymph node will be detected using a gamma-ray detection probe (NEO 2000, Johnson and Johnson) and selectively removed. After removal of the marked lymph node, an ALND will be performed. The correlation between the tumor response in the marked lymph node and tumor response in the ALND specimen will be investigated.

During this study all patients will receive an ALND and a model will be generalized to predict an axillary favorable response, which is defined as as pathological complete remission or residual micrometastasis (< 2mm). In a future study, patients with a favourable response will be treated with axillary radiation therapy instead of axillary lymph node dissection.

**Doel van het onderzoek**

The aim of this protocol is twofold.

1. Firstly, we aim to combine the new response monitoring method (PET imaging) with the present technique (dynamic CE-MRI imaging) in order to discriminate between favourable and unfavourable response of the primary tumor during and after neoadjuvant chemotherapy;

2. Secondly, we aim to investigate whether the axillary tumor response to primary systemic therapy can be reliably assessed.

**Onderzoeksopzet**

3x FDG-PET/CT (before and early during the chemotherapy course)
Iodine-125 seeds localisation of proven lymph node metastases before neoadjuvant chemotherapy and selectively removal of marked nodes after neoadjuvant chemotherapy.

**Onderzoeksproduct en/of interventie**

1. 3x FDG-PET/CT (before and early during the chemotherapy course);

2. Iodine-125 seeds localisation of proven lymph node metastases before neoadjuvant chemotherapy;

3. Selectively removal of marked nodes after neoadjuvant chemotherapy.

# Contactpersonen

## Publiek

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## Wetenschappelijk

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# Deelname eisen

## Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Proven infiltrating breast cancer with either a primary tumor over 3 cm in size (clinical examination) or cytologically proven spread to the axillary lymph nodes;

2. Stage II or stage III disease (revised AJCC staging system 2001). 'Locally advanced breast cancer' patients are consequently eligible, including those with ipsilateral supraclavicular lymph node metastases. In stage II patients with T1N1 disease, N1 status must have been demonstrated by either fine needle aspiration from an axillary lymph node or by a metastasis of over 2 mm in diameter at sentinel node biopsy. Stage IIA patients are only eligible if the tumor is over 3 cms in diameter;

3. Age 18 to 65 years; patients older than 65 years may be included when considered 'biologically 65 years or younger';

4. Performance status: WHO 0 or I;

5. Adequate bone marrow function (W.B.C. count > 3.0 x 109/l, platelets > 100 x 109/l);

6. Adequate hepatic function (ALAT, ASAT and bilirubin < 2 x upper limit of normal);

7. Adequate renal function (creatinine clearance > 60 ml/min);

8. Radionuclide ejection fraction > 0.509;

9. Informed consent.

### Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Evidence of distant metastases. Staging examinations must have included a chest roentgenogram, an ultrasound examination of the liver and an isotope bone scan. Abnormal uptake on the isotope bone scan can only be accepted if bone metastases were excluded by MRI;

2.Previous radiation therapy or chemotherapy;

3. Other malignancy except carcinoma in situ, unless the other malignancy was treated 5 or more years ago with curative intent without the use of chemotherapy or radiation therapy;

4. Pregnancy or breast feeding must be excluded and patients must use adequate contraceptive protection.

## Onderzoeksopzet

### Opzet

| | |
|---|---|
| Type: | Interventie onderzoek |
| Onderzoeksmodel: | Anders |
| Toewijzing: | N.v.t. / één studie arm |
| Blindering: | Open / niet geblindeerd |
| Controle: | N.v.t. / onbekend |

### Deelname

Nederland

| | |
|---|---|
| Status: | Werving gestart |
| (Verwachte) startdatum: | 01-07-2008 |
| Aantal proefpersonen: | 300 |
| Type: | Verwachte startdatum |

## Ethische beoordeling

Positief advies

| | |
|---|---|
| Datum: | 25-05-2009 |
| Soort: | Eerste indiening |

## Registraties

### Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 31961
Bron: ToetsingOnline
Titel:

### Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

### In overige registers

| Register | ID |
|---|---|
| NTR-new | NL1696 |
| NTR-old | NTR1797 |
| CCMO | NL23017.031.08 |
| ISRCTN | ISRCTN wordt niet meer aangevraagd |
| OMON | NL-OMON31961 |

## Resultaten

**Samenvatting resultaten**
N/A