

# Breast Density as Indicator for the Use of Mammography or MRI to Screen Women with Familial Risk for Breast Cancer: a RCT.

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To assess, based on a woman's risk profile, mammographic density and age, the most cost-effective screening method, mammography or MRI, for women at high risk.

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Recruiting
<b>Health condition type</b>	Breast neoplasms malignant and unspecified (incl nipple)
<b>Study type</b>	Observational invasive

## Summary

### ID

NL-OMON43998

### Source

ToetsingOnline

### Brief title

FaMRIsC (is for FaMiliial risk MRI SCreening indicated by breast density? )

### Condition

- Breast neoplasms malignant and unspecified (incl nipple)

### Synonym

breast cancer, neoplasm mammae

### Research involving

Human

### Sponsors and support

**Primary sponsor:** Erasmus MC, Universitair Medisch Centrum Rotterdam

**Source(s) of monetary or material Support:** KWF en ZonMW

## Intervention

**Keyword:** breast density, breast MRI, high familial breast cancer risk, screening

## Outcome measures

### Primary outcome

Primary outcomes are: the numbers of tumours detected at screening examinations and in between screening examinations (interval tumours), and the stage distribution at diagnosis in the different trial arms, with application of density scores for the analyses of results.

### Secondary outcome

Other outcomes are the sensitivities and proportions of false-positive results.

Breast cancer mortality reduction will be estimated using breast cancer microsimulation models (MISCAN). Costs will be calculated per quality adjusted life-year gained.

## Study description

### Background summary

In the Netherlands and many other countries, it is now recommended that women with a BRCA1 or 2 mutation are screened by yearly MRI between age 25-60. Less than 5% of all breast tumours are related to such mutations. Having a clear family history of breast cancer, but no BRCA1 or 2 mutation, and having dense breast tissue are both strong breast cancer risk factors conferring high risk often already at a young age. Currently the Dutch guideline recommends these women screening with mammography, although sensitivity of MRI was much higher in all risk and age groups in the Dutch MRISC and comparable international studies. Especially in women with high mammographic density, in whom breast cancer risk is highest, the sensitivity of mammography is seriously impaired, leading to many missed cases. MRI is likely to lead to better detection of breast tumours in these groups. Breast density is high in 60% of the women below age 50 yrs. But high mammographic density not only indicates a high breast cancer risk and decreased performance of mammography, but also more

benign breast disease and therefore potentially more false positive MRI-results. Cost-effectiveness may thus vary across categories of mammographic density. The limitation of all previous MRI screening studies is that they do not contain a comparison group; all participants received both MRI and mammography. Therefore, we cannot empirically assess in which stage tumours would have been detected by either test or whether MRI would reduce the number of interval tumours. We need a randomized controlled trials (RCT) to assess the gain and cost.

## **Study objective**

To assess, based on a woman's risk profile, mammographic density and age, the most cost-effective screening method, mammography or MRI, for women at high risk.

## **Study design**

A Randomised Controlled Trial, comparing a screening strategy where MRI is added to the practice according to the current guideline for women with high risk due to family history:

Women aged 30-55 years, with >20% familial CLTR but no known BRCA1 or 2 mutations.

Intervention: \*yearly MRI and clinical examination + mammography every other year\*(n=1,000) versus

(current practice) \*yearly mammography and clinical examination\* (n=1,000).

Results will be stratified by mammographic density to examine whether cost-effectiveness of the screening strategies is dependent on mammographic density.

## **Study burden and risks**

To perform MRI takes about 20 minutes, no extra visit to the centre is needed. Haematoma may occur because of the IV gadolinium contrast, for which contrast few women may be allergic.

Women will be warned that MRI may have more false-positive results, that may prompt additional ultrasound, fine needle aspiration biopsy or even histologic biopsy with local anaesthesia.

## **Contacts**

### **Public**

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## **Trial sites**

### **Listed location countries**

Netherlands

## **Eligibility criteria**

### **Age**

Adults (18-64 years)

Elderly (65 years and older)

### **Inclusion criteria**

Familial cumulative lifetime breastcancer risk of \* 20% according to Claus tables (as used by Genetic Centres)

age 30-55 yrs.

### **Exclusion criteria**

BRCA1 or BRCA2 mutation carrier or 50% risk of being one.

Personal history of breast cancer

Breast MRI contra-indication like metal implant

## **Study design**

## Design

Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

## Recruitment

NL	
Recruitment status:	Recruiting
Start date (anticipated):	17-01-2011
Enrollment:	2000
Type:	Actual

## Ethics review

Approved WMO	
Date:	08-11-2010
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	
Date:	16-01-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	
Date:	10-02-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	
Date:	18-10-2016
Application type:	Amendment

Review commission:

METC Erasmus MC, Universitair Medisch Centrum Rotterdam  
(Rotterdam)

## 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	NL32803.078.10