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.

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

Summary

ID

NL-OMON43998

Source
ToetsingOnline

Brief title
FaMRIsc (is for FAmilial 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 familal 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 occurr 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
Erasmus MC, Universitair Medisch Centrum Rotterdam

Groene Hilledijk 301

Rotterdam 3075 EA
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

Groene Hilledijk 301
Rotterdam 3075 EA
NL

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