Efficacy of Magnetic Resonance-guided High Intensity Focused Ultrasound for the Ablation of Breast Cancer

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Ethical review	Approved WMO
Status	Completed
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Interventional

Summary

ID

NL-OMON55791

Source
ToetsingOnline

Brief title
MR-HIFU breast cancer II

Condition

- Breast neoplasms malignant and unspecified (incl nipple)
- Breast disorders
- Breast therapeutic procedures

Synonym
breast cancer, malignant breast tumor

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht

Source(s) of monetary or material Support: Ministerie van OC&W,Center for Translational Molecular Medicine (CTMM) en vrienden UMC Utrecht

Intervention

Keyword: Ablation, Breast cancer, High Intensity Focused Ultrasound (HIFU), Magnetic Resonance Imaging (MRI)

Outcome measures

Primary outcome

The primary endpoint of this study is the efficacy of MR-HIFU for ablation of

breast tumors assessed by the amount of necrotic tumor tissue, which will be

determined by MRI and by histopathologic examination after resection.

Secondary outcome

The secondary endpoint is safety, assessed by reporting adverse events and by

NRS (numeric rating scale) after the MR-HIFU procedure.

Study description

Background summary

Breast-conserving therapy is standard of care for patients with localized breast cancer. Nowadays there is growing interest to treat breast cancer patients in a less invasive way, e.g. by radiofrequency, laser, microwave and high intensity focused ultrasound (HIFU) ablation. Magnetic Resonance-guided High-Intensity Focused Ultrasound (MR-HIFU) is a completely non-invasive treatment technique. HIFU uses focused ultrasound waves for tumor ablation by heating the cancerous tissue. Real time monitoring of the treatment with Magnetic Resonance Imaging (MRI) is used to ensure optimal safety. Previous MR-HIFU studies have shown low complication rates and quick recovery. Philips Healthcare developed a dedicated MR-HIFU breast system for ablation of tumors in the breast, the Philips Sonalleve MR-HIFU Breast Tumor Therapy System. In 2017 Profound Medical acquired Philips* MR-HIFU business and Profound Medical has since then taken over responsibility as manufacturer of the MR-HIFU breast system. A feasibility study in 10 patients assessing the treatment accuracy of MR-HIFU ablation of malignant breast tumors has been performed at the UMC Utrecht (METC no. 12-082). The results show that MR-HIFU ablation is a safe and

accurate treatment for malignant breast tumors. The next step is to prove the efficacy of MR-HIFU ablation with the dedicated breast system, which must be equal to conventional surgery to enable clinical implementation of this treatment.

Study objective

The main objective of this study is to demonstrate treatment efficacy of MR-HIFU ablation of breast cancer. Effective treatment is defined as 100% necrosis of the targeted primary breast tumor. The secondary objective is safety of the MR-HIFU treatment.

Study design

Single-center, single arm, non-randomized, intervention study.

Intervention

This study will be performed according to a treat-and-resect protocol. The entire breast tumor including a 5 mm safety margin will be ablated with the dedicated breast system. After 1-3 weeks, patients will undergo (breast-conserving) surgery as standard clinical practice to ensure total removal of cancerous tissue and to determine the efficacy of MR-HIFU ablation. Patients are treated under procedural sedation analgesia (PSA) with Esketamine and Propofol or Remifentanil and Propofol.

Study burden and risks

After signing informed consent, patients will undergo a conventional MRI scan (1.5 or 3.0 Tesla) with a Gadolinium-Based Contrast Agent (GBCA) at the outpatient clinic. This Dynamic Contrast-Enhanced MRI (DCE-MRI) scan is required to determine whether a patient meets all additional HIFU treatment inclusion criteria. Eligible patients will undergo HIFU treament. On the day of treatment, patients will be admitted at the Radiology department. During treatment, the patient lies in prone position on the table top of the dedicated MR-HIFU breast system, integrated in an MRI bore. An intravenous catheter will be used for the administration of sedatives and the Magnetic Resonance (MR) contrast agent and an urinary catheter will be placed. After treatment patients will be monitored in the hospital at the nursing unit of the Imaging division for a few hours and discharged on the same day, or later if clinically indicated. After one to two weeks after MR-HIFU treatment, a third DCE-MRI scan will be performed to determine radiological response of the tumor. Digital photographs of the breast will be made before and after the treatment to evaluate cosmetic effects. Optionally, three blood samples will be obtained once before and twice after the MR-HIFU procedure, if possible from an already inserted intravenous catheter (otherwise via venipuncture). The samples will be

used for future research in the field of breast cancer and/or MR-HIFU treatment, the tests are not all determined yet. Patients will undergo surgery in one to three weeks after MR-HIFU treatment. They will receive additional treatment with radiotherapy and/or chemotherapy and follow-up according to standard clinical practice. The most important risks associated with participation in this study include: thermal damage to the skin or pectoral muscle, damage to lungs or heart and complications associated with PSA.

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

• Women, aged 18 years and older.
• Able to give informed consent herself.
• World Health Organization (WHO) performance score <= 2.

• Biopsy proven cT1-2 N0-2 MX invasive breast cancer with a size of <= 3.0 cm.
• Histological type of tumor: invasive ductal carcinoma (IDC), not otherwise specified (NOS) or no special type (NST).
• The target breast fits in the cup of the dedicated MR-HIFU breast system.
• Patient weight is limited to <= 90 kg, because of restrictions of HIFU table top., Additional HIFU treatment inclusion criteria based on MRI findings:
• The tumor is located within the reach of the HIFU beam.
• The distance of the tumor, including a 5 mm margin around the tumor, from the skin, nipple and pectoral wall is at least 1.0 cm.

Exclusion criteria

• Prior treatment with: neo-adjuvant systemic therapy in the past 3 months or radiotherapy or thermal therapy or surgery of any kind in the targeted breast.
• Contraindications to MR imaging according to the hospital guidelines (e.g. pacemaker in situ, severe claustrophobia, big metal implants, body size incompatible with MR bore).
• Contraindications to administration of gadolinium-based contrast agent, including: prior allergic reaction to any contrast agent, renal failure (GFR < 30 ml/min/1,73m2).
• Contra-indications for procedural sedation analgesia with Propofol and Eskatamine or Propofol and Remifentanil.
• Extensive intraductal components in the lesion determined by biopsy, defined as a ratio of more than 0.5 when dividing the number of ducts or lobules involved with carcinoma in situ by the number of tissue cores in the biopsy.
• Scar tissue or surgical clips in the HIFU beam path.
• Inability to lie in prone position.
• Pregnancy or lactation.
• Communication barrier with patient.
• N0, Her2neu negative, <35 years, <=1cm (T1a/b) with B&R grade 1 or 2 on biopsy.
• N0 Her2neu negative, ER/PR negative (triple negative), 35-70yr, 1.1-2cm (T1c) with B&R grade 1 or 2 on biopsy.
• N0, Her2neu negative, ER/PR positive > 50%, ductal carcinoma, 60-70yr, 1.1-2cm (T1c), with B&R grade 3 on biopsy and if the MammaPrint is not reimbursed by health insurance also for grade 1 on biopsy.
• N0, Her2neu negative, ER/PR positive, ductal carcinoma, 35-60yr, 1.1-2cm (T1c), with B&R grade 1 on biopsy.
• N0, Her2neu negative, ER/PR positive, but <=50%, ductal carcinoma, 60-70yr, 1.1-2cm (T1c) with B&R grade 1., • Only if the MammaPrint is reimbursed by health insurance: N0, Her2neu negative, ER/PR positive, > 50% ductal carcinoma, 60-70yr, 1.1-2cm (T1c), with B&R grade 1 and MammaPrint high risk.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	15-05-2017
Enrollment:	50
Type:	Actual

Medical products/devices used

Generic name:	High intensity focused ultrasound ablation with the MR-HIFU breast system
Registration:	No

Ethics review

Approved WMO Date:	05-12-2014
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	16-02-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-03-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	20-10-2021
Application type:	Amendment
Review commission:	METC NedMec

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
ClinicalTrials.gov	NCT02407613
CCMO	NL46863.041.14

Study results

Date completed: 30-09-2024

Summary results
Trial ended prematurely