Phase III, Multicenter, Double-blind, Randomized, Crossover Study to Compare MultiHance with Magnevist in Contrast-Enhanced Magnetic Resonance Imaging (MRI) of the Breast.

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Primary Objective: To show superiority of a 0.1 mmol/kg dose of MULTIHANCE over a 0.1 mmol/kg dose of MAGNEVIST for breast MRI in terms of sensitivity for the diagnosis of malignant lesions compared with histopathology. Secondary Objectives: a)To...

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

Summary

ID

NL-OMON30924

Source
ToetsingOnline

Brief title
DETECT

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
breastcancer, mammacarcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Bracco-Byk
Source(s) of monetary or material Support: Bracco

Intervention

Keyword: breast, contrast-enhanced, double-blind, MRI

Outcome measures

Primary outcome

Diagnostic performance of MULTIHANCE and MAGNEVIST will be evaluated by comparing the off-site evaluation results of MRI with the truth standard findings. Sensitivity, specificity, accuracy, positive predictive value and negative predictive value of breast MRI performed with MULTIHANCE or MAGNEVIST will be analyzed independently against the truth standard findings at lesion, region, breast and subject levels. The primary endpoint of this study will be sensitivity with the hypothesis of superiority of MULTIHANCE over MAGNEVIST for breast MRI in the diagnosis of breast cancer. Only lesions confirmed as malignant by histopathology will contribute to the primary analysis.

Secondary outcome

Measures of diagnostic performance for each MRI examination will also be calculated at region, breast and subject levels and compared as secondary endpoints.

Study description

Background summary

Magnetic resonance imaging (MRI) is rapidly emerging as a clinically useful

examination for the evaluation of breast lesions because of its value in soft tissue assessment. It is well accepted that the use of intravenous MRI contrast agents contributes to the detection as well as the characterization and delineation of breast lesions. Preliminary investigations with MULTIHANCE in breast MRI have demonstrated promising results. With the experience gathered from a study in 189 subjects, the 0.1 mmol/kg dose appeared superior to the 0.05 and 0.2 mmol/kg doses in both lesion detection and characterization. Based on these results, the optimal dose selected for breast studies is 0.1 mmol/kg. No safety concerns were raised in subjects receiving up to a dose of 0.2 mmol/kg MULTIHANCE.

Study objective

Primary Objective: To show superiority of a 0.1 mmol/kg dose of MULTIHANCE over a 0.1 mmol/kg dose of MAGNEVIST for breast MRI in terms of sensitivity for the diagnosis of malignant lesions compared with histopathology. Secondary Objectives: a)To compare the 0.1 mmol/kg dose of MULTIHANCE with the 0.1 mmol/kg dose of MAGNEVIST for breast MRI for the diagnosis of breast cancer compared with truth standard findings in terms of: sensitivity, specificity, accuracy, positive predictive value and negative predicative value at region level, at breast level; and at subject level; and inter-reader agreement in determining the nature of the lesions; b)To compare the 0.1 mmol/kg dose of MULTIHANCE with the 0.1 mmol/kg dose of MAGNEVIST for breast MRI in terms of: qualitative and quantitative assessment of contrast between breast lesions and normal parenchyma, Qualitative assessment of border delineation of lesions, and global diagnostic preference of the blinded readers; c)To confirm the previously established safety profile of a single dose (0.1 mmol/kg) of MULTIHANCE in comparison with MAGNEVIST at the same dose for MRI of the breast.

Study design

This will be a Phase III, multicenter, randomized, double-blind, crossover study aimed at within subject comparison of 0.1 mmol/kg MULTIHANCE and 0.1 mmol/kg MAGNEVIST during breast MRI examinations in subjects with suspected or known breast cancer in terms of diagnostic and technical performance in the diagnosis and evaluation of malignant and benign breast lesions as determined by histopathology. In case of benign lesion(s) not confirmed at histopathology, ultrasound and/or mammography will be performed at 6-month (+ or - 2 months) after Exam 2. Each subject will undergo two breast MRI examinations (Exam 1 and Exam 2) with a minimum interval of 48 hours, but no longer than 14 days between the examinations, using commercially available equipment at 1.5 Tesla (T) magnetic field strength. All MRI image sets of the subjects included in the study will be collected for both on-site and independent off-site evaluations. The Investigators at each site will evaluate the MRI images from Exam 1 and Exam 2, respectively. An additional independent Investigator, other than the MRI reader, will provide all truth standard findings. Off-site assessments of

MRI will be conducted by 3 independent experienced radiologists unaffiliated with the study sites and fully blinded to all clinical and radiological information of the subjects and the IP used in each respective MRI examination. After the off-site blinded read is completed, adjudication will be performed by an additional independent experienced radiologist (adjudicator) unaffiliated with the study sites.

Intervention

In Exam 1, 50 % of the patients start with MultiHance, the others with Magnevist. In Exam 2 the patients get the other contrast liquid in comparison with Exam 1.

Study burden and risks

Both MULTIHANCE and MAGNEVIST, have very good and similar safety profiles. MRI is a standard non-invasive clinical diagnostic imaging technique that does not involve ionizing radiation. The risk of undergoing MRI examination is extremely low if the standard precautions and procedures are to be followed and subjects with contraindications to MRI or test agents are excluded from this study. Expected benefits from the MRI examinations include more reliable diagnosis than conventional imaging techniques such as mammography or ultrasonography.. MRI contrast agents will be injected intravenously which may carry a common risk related with venipuncture, such as discomfort and/or bruising at the site of puncture.
It is not possible to predict whether or not any direct benefit may result from the participation in this study. Diagnostic contrast agents are usually studied in single-administration trials. However, the crossover trials conducted so far with MULTIHANCE in comparison with MAGNEVIST have not shown any overall increased incidence of adverse events. Therefore, no substantial added risk is foreseen when two contrast-enhanced MRI examinations are performed on the same subject with a minimum interval of 48 hours. Conversely, on the basis of the recent results of intra-individual comparison of MULTIHANCE with MAGNEVIST in breast MRI, some benefit due to additional imaging with MULTIHANCE and careful diagnostic evaluation could be expected for some subjects of the present study in terms of more accurate detection or diagnosis of breast cancer.

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

written Informed Consent
Female subject of 18 years or older
At least one suspicious or known breast lesion
Is planned to undergo histological diagnosis of breast lesions

Exclusion criteria

Subject:
-has body weight > 100 Kg
-is pregnant or lactating
-has severe or end-stage organ failure
-has moderate to severe renal impairment
-is undergoing or has undergone radiotherapy within 18 months before exam 1
-is undergoing or has undergone chemotherapy/antitumural hormonal therapy within 6 months before exam 1
-has recieved or scheduled to receive any onther contrast medium 24 hours before or after exam1

-has history of breast surgery

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-09-2007
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	27-04-2007
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-06-2007
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
EudraCT	EUCTR2006-004613-18-NL
CCMO	NL16938.060.07