Primovist enhanced MRI for the detection and evaluation of focal liver lesions

Published: 23-03-2009
Last updated: 06-05-2024

Primary Objective: Sensitivity, specificity and positive predictive value (PPV) for the detection and characterization of focal liver lesions using Gd-EOB-DTPA contrast or DWI with TRONSecondary Objective(s): 1) Differences between sensitivity,...

Ethical review	Not approved
Status	Will not start
Health condition type	Hepatobiliary neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON33584

Source
ToetsingOnline

Brief title
PRIDE-study

Condition

- Hepatobiliary neoplasms malignant and unspecified

Synonym
focal liver lesion, focal liver tumor

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Bayer,een grant van Bayer Schering Pharma opdat de uitvoering van het onderzoek gefinancierd kan worden

Intervention

Keyword: Characterization, Detection, Focal liver lesions, Primovist MRI

Outcome measures

Primary outcome

The main study parameters are sensitivity, specificity and positive predictive

value for the detection and characterization of focal liver lesions

Secondary outcome

Sensitivity and specificity for the detection of hypo- and hypervascular lesions

Sensitivity and specificity for the characterization between benign and

malignant lesions

Difference in ADC-value between benign and malignant lesions

Study description

Background summary

In patients with liver cancer or other liver lesions, liver imaging is crucial to establish the extent and nature of the tumour(s). These two factors are essential to define the therapeutic strategy or intervention.
MR imaging has been through major developments the last decade with an increase in contrast agents and new MR sequences.
Contrast enhanced MRI has shown to be a very high-quality detection tool for focal liver lesions, with even higher sensitivities for the detection of focal liver lesions than CT5-8. Recently, new MR contrast agents have been developed to increase the sensitivity for the detection and characterization of focal liver lesion. Primovist (Gd-EOB-DTPA, Gadoxetic acid, Bayer Schering Pharma, Berlin) is one of these new, highly specific MRI contrast agent for the imaging, detection and characterization of liver pathology, including liver tumors, cysts, as well as other malignant and benign lesions. Primovist has a water-soluble compound which is taken up by the hepatocytes (approximately 30%) and is equally excreted renal and biliary in humans*.
Primovist enhances the signal of T1 weighted MR images immediately after

administration. The hepatocytes uptake will increase the signal intensity of normal liver parenchyma. This results in improved lesion-to-liver contrast because malignant tumors (metastases, HCC) do not contain either hepatocytes or their functioning is hampered*. Furthermore, as this agent is specific for hepatocytes, it is postulated that lesions such as Focal Nodular Hyperplasia (FNH) can be better distinguished form lesions such as adenoma or HCC. After administration of Primovist a dynamic phase scans can be performed in arterial phase, portal-venous phase and equilibrium phase.
Apart from the new contrast agents, there are also major advances in MR sequences, including Diffusion Weighted Imaging (DWI). DWI is an excellent MR tool for the detection of pathological lesions, and is increasingly applied for tumour evaluation in the abdomen and pelvis.
Diffusion Weighted Imaging originates from the T2 weighted images and uses the motion of protons in the extracellular space by using large bipolar gradients to differentiate between different tissues. This signal is converted to a high or low signal intensity on the MR-images. For example, normal liver parenchyma has a certain motion which correlates to a large diffusion and therefore low signal on MRI (white), while tumor tissue a much smaller diffusion and therefore gives a high signal on MRI (dark). The motion of the extracellular protons is called the apparent diffusion coefficient (ADC). With malignancy, the extracellular space is decreased resulting in a decrease in ADV value. Benign lesions like cysts normally show an increase in extracellular space which results in an increase in ADV value. The value of the ADC can therefore be used to distinguish between normal liver parenchyma and focal liver lesions9,10.
There are different DWI sequences, with b=50 s/mm2 and b=500 s/mm2 regularly used. B=50 will provide improved anatomical information and has a high sensitivity for the detection of lesions. B=500 improves the specificity for lesion characterization, meaning that malignant lesions emphasize on this image, while benign lesions don*t.
Respiratory triggered DWI can also be performed after bolus injection of a contrast agent. In this study we will administer Primovist. We will compare the sensitivity and specificity for the detection and characterization of focal liver lesions for contrast enhancement with Primovist alone and for DWI alone. Furthermore we are especially interested in changes in ADC value between benign and malignant lesions.

Study objective

Primary Objective:
Sensitivity, specificity and positive predictive value (PPV) for the detection and characterization of focal liver lesions using Gd-EOB-DTPA contrast or DWI with TRON

Secondary Objective(s):
1) Differences between sensitivity, specificity and PPV for the detection and characterization of benign and malignant lesions

2) Differences between sensitivity, specificity and PPV in the detection between hypo- and hypervascular lesions
3) Accuracy for the characterization of lesions
4) Differences in apparent diffusion coefficient (ADC) value between benign and malignant lesions larger than 1 cm

Study design

This is a prospective cohort study.

Study burden and risks

After inclusion, each patient will receive two liver MRI*s: one MRI with Gadovist enhancement, one MRI with Primovist enhancement. Since all these patients were referred to the Radiology Department for a Gadovist enhanced MRI of the liver, only the Primovist enhanced MRI is associated with an extra burden. The Diffusion Weighted Imaging images do not increase any risk or burden.
After inclusion in this study, one follow-up MRI scan with Gadovist enhancement will be performed 6 months after the primary MRI, or 6 months after surgery for the operable patients, which may differ from the standard follow-up. This investigation is complementary to this study, although Gadovist is the standard of care momentarily in the UMC Utrecht.
Primovist is a registered contrast agent with no more side effects than Gadovist, therefore no more (serious) adverse effects or (serious) adverse reactions are expected to occur compared to the standard liver MRI with Gadovist. Bayer Schering pharma has extensively tested Primovist for its safety within phase 1,2 and 3 studies1-4.
In 10.3% of patients receiving Primovist AE*s are expected1,2. The most frequent AE*s that occur are headache and nausea with an incidence of 1.1%, which is comparable to other Gadolineum contrast agents*. No other AE*s show any incidence higher than 1.1%*. No deaths are reported in phase 2 and 3 studies due to the administration of Primovist2,*. SAE*s were classified according to the ICH-GCP definition and included any event resulting in death, were life-threatening, required inpatient hospitalization/prolonged existing hospitalization or resulted in persistent significant disability/incapacity or a congenital birth defect. SAE*s were seen in 3.3% of patients with AE*s and in 0.3% (6/1755) of total population*.
Apart from the MRI investigations, each patient will be called by the study coordinator one month and six months after the Primovist enhanced MRI, to determine if any (S)AE occurred during the study period.
No other investigations, time-consuming events, questionnaires or visits to the hospital are necessary when participating in this study.
Participation in this study will result in a close and thorough investigation of the patients* liver disease.

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

1) Suspicion of focal liver lesions, both benign and malignant
2) Age > 18 years

Exclusion criteria

- clinical query on liver MRI chart directed to other liver disease than focal liver lesions like cirrhosis, hepatitis or liver abces
- previous liver surgery
- a pacemaker
- administration of a liver specific contrast agent within 2 weeks prior to the first MRI with Primovist

- claustrophobia
- hypersensitivity to active substance or any of the recipients of Gd-EOB-DTPA contrast
- caution should be exercised in patients with clinically severe cardiovascular disease. myocardial infarction, uncontrolled hypertensia, instable angina pectoris, congestive hert failure, uncontrolled arhythmia's requiring medication
- severe kidney failure (creatinin clearance <30ml/min)
- pregnancy or lactating women
- high plasma concentration of rifampicin (inhbitor of Gd-EOB-DTPA uptake)

Study design

Design

Study phase:	4
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	125
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Generic name:	Paramagnetic contrast agent (Primovist)

Ethics review

Not approved

Date:	10-03-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2008-004992-22-NL
CCMO	NL24865.041.08