PROspective Multi-center study to Evaluate the correlation between safety margin and local recurrence after THErmal ablation USing image co-registration in patients with hepatocellular carcinoma (PROMETHEUS-study)

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Hepatobiliary neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON55994

Source
ToetsingOnline

Brief title
PROMETHEUS

Condition

- Hepatobiliary neoplasms malignant and unspecified
- Hepatobiliary neoplasms malignant and unspecified
- Hepatobiliary therapeutic procedures

Synonym
hepatocellular carninoma, liver cancer

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: KWF Kankerbestrijding

Intervention

Keyword: hepatocellular carcinoma, local recurrence, safety margin, thermal ablation

Outcome measures

Primary outcome

To determine the minimal ablation margin required to achieve a local recurrence

rate of < 10% in patients undergoing thermal ablation for HCC

Secondary outcome

- To analyze the correlation between ablation margins and local recurrence in

patients undergoing thermal ablation for HCC

- To assess the efficacy of thermal ablation in a large cohort of HCC patients

Study description

Background summary

Compared to thermal ablation, the complication rate in surgically treated HCC patients is much higher with an odds ratio of 8.24 (95% CI: 2.12-31.95). Yet, surgical resection yields better results regarding local recurrence (HR 0.38 (95% CI: 0.17-0.84)). Therefore, surgical resection remains the treatment of choice for most patients with BCLC 0/A HCC, despite higher morbidity and mortality rates. For thermal ablation to become truly competitive with surgical resection, the issue of local recurrence needs to be addressed. Ablation systems have predefined algorithms, based on in vitro experiments, to predict size and shape of the ablation. In general, ablations setting are

chosen that would result in complete tumor ablation with a safety margin of >5mm, but the actual ablation zone may be smaller than expected and deformed as a result of factors such as inhomogeneous tissue density, liver cirrhosis and heat-sink.
After surgical resection, a pathologist examines the resected specimen to confirm complete resection. After ablation, confirmation of successful ablation can only be obtained using imaging modalities. Currently there is no validated, standardized method to accurately determine safety margins. Most commonly, the interventional radiologist performing the procedure estimates the safety margins by visual qualitative assessment of pre- and post-ablation contrast-enhanced CT (CECT). This method is associated with high interobserver variability and lacks accuracy. There is a need for a method that allows more accurate assessment of safety margins after ablation.

Study objective

Over recent years, post-processing software has become available that allows co-registration of pre- and post-ablation CECT. This allows three-dimensional quantitative assessment of ablation margins. Such quantification of ablation margin would allow immediate evaluation of ablation margins and reablation during the same treatment session if margins are deemed to be insufficient. It would potentially be the equivalent of the frozen section that is used for real-time margin control during surgery.
Retrospective studies have demonstrated the potential value of quantitative assessment of ablation margins after thermal ablation, but this has neither been validated in prospective studies nor in larger patient groups. In a prospective, multi-center, non-experimental study in patients undergoing ablation for BCLC 0/A/B HCC, safety margins will be quantitatively assessed using dedicated co-registration software.
The aim of this project is to correlate ablation margins with outcome to determine the relationship between ablation margins and local recurrence and set the optimal threshold for minimal ablation margin.

Study design

Multicentre study in patients with early stage HCC (BCLC 0 / A) undergoing ablation. All patients receive one
treatment according to the applicable standard of the participating center. Patients are treated under overall
anesthesia or under deep sedation. During the procedure, a CT is performed both before and after the ablation. The treating
The doctor determines in a standard manner whether the treatment has been successful (in most centers a visual estimate is made
made whether the tumor has burned away sufficiently widely). After the procedure, the scans are sent to the Leiden University
University Medical Center (LUMC). The scans are used to determine the safety

margin for each patient
was achieved with the help of the deLIVERed computer program developed by the LUMC. Patients will be over time
continued, collecting data on, among other things, the occurrence / non-occurrence of a local recurrence and survival.
LUMC, Radboud MC, Erasmus MC, Amsterdam MC, UMCU, MUMC +, UMCG and HMC are participating in the research. It
research is supported by the Dutch Liver Patient Association, the Dutch hepatocellular Carcinoma Group,
Dutch oncology Research Platform and the Dutch Association for Intervention Radiology.

Study burden and risks

This study is considered an intermediate risk trial. Patients may undergo an additional CT of the upper abdomen (in same centers this is standard of care as the pre-ablation CT is used for needle placement). The additional CT carries a low risk of additional radiation and increased dose of contrast medium.
The additional CT will be performed during the ablation procedure with the patient under general anesthesia or conscious sedation. Besides the additional CT, patients will receive standard of care. Thermal ablation and follow-up will be performed according to the standard protocol of the participating center.
We expect that this project will result in a clear understanding of the correlation between ablation margins and local recurrence. Using co-registration software, we will then, in future patients, be able to estimate the risk of local recurrence in patients undergoing ablation for HCC. Immediate re-ablation may be performed in patients with insufficient margins. The long-term objective is to reduce local recurrence rates after thermal ablation.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- Age 18 yrs or above
- HCC very early (0) or early stage (A) according to the BCLC staging system OR HCC intermediate stage (B) with a maximum of two lesions of <=5cm each
- Either de novo or recurrent HCC (prior locoregional therapy is allowed in the study)
- Candidate for percutaneous thermal ablation as discussed in a multidisciplinary tumor board
- Absence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule
- Written informed consent

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Estimated GFR <30 ml/min
- Known severe allergy to contrast medium
- ASA classification higher than 3
- Child Pugh C
- ECOG >=1 (tumor-related)
- Portal vein tumor invasion
- Extrahepatic metastasis
- Neoadjuvant transarterial therapy (TACE, TAE or TARE), i.e. combination therapy of transarterial therapy with ablation

- Uncorrectable coagulopathy

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-10-2021
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO

Date:	23-08-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	29-04-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	31-08-2023

Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	02-09-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 25324
Source: NTR
Title:

In other registers

Register	ID
ClinicalTrials.gov	NCT04123340
CCMO	NL75744.058.21