Selective Indocyanine Green Injection of a Segmental Hepatic Artery Followed by Near-Infrared Fluorescence Guided Anatomical Liver Resection: A Feasibility Study

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Primary objective: To investigate the feasibility of using intraarterial ICG preoperatively to allow for liver segment visualization during anatomical liver resection.Secondary Objective(s): 1. To investigate the dosage which provides sufficient...

Ethical review	Approved WMO
Status	Completed
Health condition type	Hepatobiliary neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON52161

Source
ToetsingOnline

Brief title
SELECT Study

Condition

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

Synonym
liver cancer, Liver tumor

Research involving

Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Anatomical liver resection, Indocyanine green, NIR fluorescence

Outcome measures

Primary outcome

The feasibility of using intra-arterial ICG and embolization preoperatively to allow for liver segment visualization during anatomical liver resection. Visibility will be measured using a contrast ratio between normal liver parenchyma and ICG colored liver parenchyma. A signal-to-background ratio of 1.6 provides sufficient contrast for an anatomical resection and will therefore be used as endpoint.

Secondary outcome

- The optimal dosage for a sufficient signal-to-background ratio

- The optimal timing of ICG administration for a sufficient signal-to-background ratio

Study description

Background summary

Anatomical liver resections for hepatocellular carcinomas (HCCs) reduce tumor recurrence and may reduce blood loss and bile leakage. Intraoperative Indocyanine green (ICG) injected through the portal vein combined with fluorescent near infrared imaging has proven to improve precision of anatomical resection. However, intraoperative portal vein administration of ICG can be

challenging, especially in laparoscopic procedures. Recent feasibility studies showed promising results for intra-arterial selective ICG injection followed by embolization of the segmental artery using intervention radiology and hybrid operating rooms. Unfortunately, hybrid operating rooms are not available in all hospitals. Therefore, our intent is to perform the interventional radiological procedure separately, before the operation to facilitate access to the procedure, logistics, safe precious personnel and time. This approach is based on the results published in a case report recently.

Study objective

Primary objective: To investigate the feasibility of using intraarterial ICG preoperatively to allow for liver segment visualization during anatomical liver resection.

Secondary Objective(s):
1. To investigate the dosage which provides sufficient contrast index of ICG in the liver segment compared to normal liver tissue.
2. To investigate the optimal timing of administration of the ICG-mixture without being washed out of a liver segment.

Study design

Prospective, single center, open-label, non-randomized phase II trial. Total of 12 patients receiving the same treatment.

Intervention

Patients will receive preoperative angiography at least three hours before the operation, during which the artery of the segment(s) containing the tumor will be selectively catheterized with a microcatheter. Angiography and cone-beam CT are then performed to confirm that the correct segment has been catheterized. A mixture of ICG and lipiodol can then be injected to stain the segment. Lipiodol causes temporary vessel occlusion as recanalization of the artery usually occurs several days to weeks after the injection. After injection of this mixture, gel foam (Cutanplast®) will be injected to avoid wash-out of ICG. Segmentectomy of the targeted liver segment(s) will then be performed using near infrared cameras for identification of the segment(s).

Study burden and risks

The burden for patients is low. In the first part no extra visits are necessary for this study, since both the interventional radiology procedure and the surgery will be performed on the same day. In the second part of the study, the interventional radiology procedure will take place one day prior to surgery; thus leading to one additional admission day. Moreover, no extra blood samples,

physical examinations, questionnaires or other tests will take place. However, in addition to the standard surgical procedure, the interventional radiologist will insert a femoral artery line in order to administer ICG, lipiodol and gel foam. Percutaneous transarterial angiography and embolization both carry the risk of mild complications like hematoma of the inguinal region or an aneurysma spurium as a result of the femoral artery puncture. With the use of a vascular closure device, the risk of puncture site complications is approximately 1%. In rare cases a dissection of the femoral, iliac or hepatic artery can occur. According to literature the chance is less than 2%.

ICG has been safely used for over 60 years for different indications. Only mild allergic reactions have been seen. Patients with a known allergic reaction to ICG or a substance related to ICG are excluded. Patients meeting one or more of the contraindications for ICG are excluded from this study.
Lipiodol is an oil-based radiopaque contrast agent of iodine combined with ethyl esters of fatty acids of poppy seed oil. Lipiodol is indicated for hysterosalpingography in adults, lymphography in adults and children and for selective intra-arterial use for imaging hepatocellular carcinoma. Patients with a known allergic reaction to lipiodol or a substance related to lipiodol are excluded from participating in this study. Patients meeting one or more of the contraindications for lipiodol are excluded from this study.
The combination of ICG and lipiodol has been studied in renal cancer and pulmonary cancer patients, without any reported adverse events.

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. Scheduled for open or laparoscopic anatomical liver resection;
2. Patients aged over 18 years old;
3. Has the ability to communicate well with the investigator in Dutch or English and willing to comply with the study design;
4. Signed informed consent prior to any study-mandated procedure.

Exclusion criteria

1. Previous major abdominal surgery 2. Known allergy or history of adverse reaction to ICG, lipiodol, gel foam, iodine or iodine contrast agents; 3. Child Pugh B or C 4. Portal hypertension or portal vein thrombosis 5. eGFR: <30; in case of eGFR 30-59 metformin should be stopped >48 hours prior to Lipiodol administration and continued >48 hours after Lipiodol administration 6. Hyperthyroidism or a benign thyroid tumor; 7. Pregnant or breastfeeding women; 8. Scheduled for palliative surgery or terminally ill 9. Any condition that the investigator considers to be potentially jeopardizing the patient*s well-being or the study objectives (following a detailed medical history and physical examination); 10. Subject taking phenobarbital, phenylbutazone, primidone, phenytoin, haloperidol, nitrofurantoin, and/or probenecid; 11. Emergency surgery.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	12-05-2022
Enrollment:	12
Type:	Actual

Medical products/devices used

Generic name:	Near-infrared fluorescence imaging system
Registration:	Yes - CE intended use
Product type:	Medicine
Brand name:	Indocyanine Green
Generic name:	sodium 4-[2-[(1E,3E,5E,7Z)-7-[1,1-dimethyl-3-(4-sulfonatobutyl)benzo[e]indol-2-ylidene]hepta-1,3,5-t
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Lipiodol
Generic name:	Ethiodized oil
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	18-10-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	08-02-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	30-06-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	30-06-2022
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	12-07-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	22-07-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	15-09-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	23-09-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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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: 21492
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2021-000270-28-NL
CCMO	NL75171.058.21
Other	NL9004
OMON	NL-OMON21492