TOTAL LIVER VOLUME CT PERFUSION AFTER AUTOMATED 3D IMAGE FUSION: A NOVEL IMAGING TECHNIQUE FOR EARLY DETECTION OF OCCULT COLORECTAL LIVER METASTASES AND IMPROVED VISUALIZATION OF LOCAL TUMOR EXTENT IN PATIENTS WITH COLORECTAL LIVER METASTASES

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

Summary

ID

NL-OMON30783

Source
ToetsingOnline

Brief title
TOTAL LIVER VOLUME CT PERFUSION AFTER AUTOMATED 3D IMAGE FUSION

Condition

- Hepatobiliary neoplasms malignant and unspecified

Synonym
Colorectal liver metastases - Liver metastases Colon or rectal cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: CT, Liver, Perfusion, Tumors

Outcome measures

Primary outcome

nvt

Secondary outcome

nvt

Study description

Background summary

Introduction & purpose
The visualization of typical hypodense colorectal liver metastases on portovenous phase CT images is often preceeded by a hyperdense blush on arterial phase CT. This is a direct result of the increased peritumoural angiogenesis surrounding an occult liver metastasis due to the local elevation of cytokines such as vascular endothelial growth factor (VEGF). Dynamic perfusion CT has previously shown to detect liver metastases in an earlier stage, especially due to an elevated microvessel density surrounding the occult metastases which leads to increased perfusion values [1]. However at the moment conventional CT perfusion is restricted to the evaluation of 2 * 3cm of axial slice thickness through the liver [2, 3]. Conventional portovenous phase CT images only show the hypodense (partially) necrotic regions of the liver lesions, whereas CTP also depicts the highly angiogenetic rim of the liver metastases [4]. Therefore, although it is unclear whether it represents reactive liver parenchyma or true tumour tissue, CTP might better delineate the

true local tumor extent into the surrounding tissues. The purpose of this study is to compare routine multiphase (4-phase) CT images of the liver with ultra-fast total volume multiphase (12-phase) dynamic CTP of the liver for the detection of small and occult liver metastases and for local tumour extent, using automated 3D image fusion, taking the intraoperative inspection and ultrasound, performed maximum 24 hours after the scan, as the gold standard. A secondary goal will be the correlation with histology (after surgical resection of liver lesions) in which we hope to determine whether the rim of high arterial perfusion surrounding liver metastases represents reactive normal liver parenchyma or true tumour tissue.

Materials and methods

Patient Selection:

A total number of 15 patients suitable for surgical resection and/or radiofrequency ablation of liver metastases will be included and examined maximum 24 hours before celiotomy after which the liver is investigated by both visual and palpatory inspection of the liver and intraoperative ultrasound (IOUS). Inclusion criteria are a WHO performance status of 0-2 [2], adequate cardiopulmonary function as well as adequate haematological, renal and hepatic function. Patients with a known contrast allergy, patients unable to hold their breath for a sufficient period of time and patients unable to obey breath-hold commands will be excluded.

Imaging Protocol:

The dynamic CT perfusion measurements will be obtained on a 64-slice multi-detector CT scanner (Somatom Sensation, Siemens, Erlangen, Germany). A twelve phase scan is acquired before and 11-times after rapid intravenous injection (6ml/s) of 100 ml low-osmolar non-ionic contrast agent with an iodine concentration of 300mg/ml (Ultravist-300 Iopromide; Schering A.G., Berlin, Germany) and 20ml saline chasing bolus into the left antecubital vein using an injection pump through an 18g needle. To start the post-contrast scans, bolus tracking (threshold 100 H.U.) is used placing a region of interest (ROI) in the right atrium. With a minimal interscan delay of 4 seconds in between two series the 1st four series were obtained in one single breath-hold at maximum inspiration. After these first series one breath out and breath in again command (lasting 8 seconds) was given before adding two series again in one single breath-hold at maximum inspiration, this was repeated until a total of twelve series were acquired. The tenth series (considered as the portovenous phase series) consists of a single breathhold scan in which the entire (upper and lower) abdomen is scanned at conventional tube voltage and current (120kV and maximum 180mAs with dose modulation). In all other series a fixed lower tube current is used to reduce radiation exposure (120kV and 80mAs). All images are initially reconstructed using thin overlapping axial slices for optimal visualization in the multiplanar reconstruction mode of the 3D fusion program.

Postprocessing:

Image fusion will be performed with a commercially available 3-D image fusion

program (Leonardo Working Station, Siemens, Erlangen, Germany). The twelve series are fused by automated (either fully automated or by using reference points) and/or manual image shifting using both coloured transparent image overlay methods and image subtraction techniques [Fig. 2]. The tenth and portovenous phase series will be chosen as reference.

For quantification of liver tissue perfusion and for the creation of blood flow maps the software program Basama Perfusion 3.0.4.8 (Kanazawa, Ishikawa, Japan) [5] will be used. This program estimates tissue perfusion as the maximum slope of the tumour time-density curve divided by the peak arterial enhancement [7, 8].

The mathematical technique has previously been fully described elsewhere [6]. Due to the dual blood supply of the liver, hepatic tissue perfusion is divided into hepatic artery and portal vein perfusion as the maximum slope of the tumour time-density curve before versus after the splenic peak enhancement divided by respectively the peak aortic and portal enhancement.

Potential risks and side-effects
Since the dynamic CTP scan will fully replace the 4-phase CT as pre-operative evaluation within this study only the additional risks and side-effects due to the different scanning protocol and contrast administration will be described. Because the 4-phase CT images can be fully deducted from the 12-phase CT images within the CTP protocol no disadvantages in the pre-operative evaluation are to be expected, although the lower mAs in 3 out of 4 phases might somewhat decrease the image quality. Nevertheless, the most important phase for morphology of the lesions and therefore the pre-operative evaluation remains the portovenous phase at which conventional kV and mAs will be used for optimal image quality.

Adverse effects & other effects of the contrast administration protocol:
Since in the routinely used 4-phase CT scan for the pre-operative evaluation the same amount and same contrast material is administered, no additional adverse effects are to be expected in this novel imaging protocol. In the CTP protocol the rate of contrast administration is somewhat higher (6ml/sec compared to the conventional rate of 3 - 4ml/sec). In the literature and in our extended experience with this injection rate no additional side effects have ever been described or seen. Nevertheless, patients with a history of cardiopulmonary disease or deteriorated cardiac function will be excluded to avoid theoretical cardiac decompensation or pulmonary oedema due to the small but rapid increase of the total circulating volume.

Radiation dose:
Dynamic CT scans will be performed with a tube currrent of 80mAs to reduce radiation exposure to patients and to improve contrast resolution of iodine based contrast agents. Again the CTP scans will replace the conventional 4-phase CT scans since all of these four phases can be deducted from the CTP

scan. The effective dose as computed according to the Monte Carlo simulations for anthropomorphic phantoms (CT-Expo; G. Stamm, Medizinische Hochschule, Hanover, Germany) and expressed according to the International Commission on Radiological Protection recommendations [7] is approximately 24,0mSv (11 x 1.5mSv + 1 x 7.5mSv) for the dynamic CTP and 20.7mSv for the routinely used 4-phase CT abdomen (3 x 4.4mSv + 1 x 7.5mSv). Therefore the additional radiation exposure compared to the conventional 4-phase CT scans in these patients is +15.9%.

Study objective

The purpose of this study is to compare routine multiphase (4-phase) CT images of the liver with ultra-fast total volume multiphase (12-phase) dynamic CTP of the liver for the detection of small and occult liver metastases and for local tumour extent, using automated 3D image fusion, taking the intraoperative inspection and ultrasound, performed maximum 24 hours after the scan, as the gold standard. A secondary goal will be the correlation with histology (after surgical resection of liver lesions) in which we hope to determine whether the rim of high arterial perfusion surrounding liver metastases represents reactive normal liver parenchyma or true tumour tissue.

Study design

nvt

Study burden and risks

nvt

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

Patients with colorectal liver metastases
Potentially curative local surgical or ablative therapy possible

Exclusion criteria

Iodine allergy
Impaired renal function
Impaired cardiopulmonary function
Impaired hepatic function
Patients unable to hold their breath for 30s or unable to obey commands

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2007
Enrollment:	15
Type:	Anticipated

Ethics review

Approved WMO
Application type:	First submission
Review commission:	METC Amsterdam UMC

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
CCMO	NL15784.029.06