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Treatment response after radioembolisation in patients with hepatocellular carcinoma—An evaluation with dual energy computed-tomography

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ABSTRACT

Purpose: The aim of this prospective study was to examine the diagnostic value of dual-energy CT (DECT) in the assessment of response of HCC after radioembolisation (RE).
Material and methods: 40 HCC patients with 82 measurable target lesions were included in this study. At baseline and follow-up examination target lesions were evaluated with (IU), AASLD and Choi measurement criteria. Disease control was defined as the sum of complete response (CR), partial response (PR), progression disease (PD) and stable disease (SD).
Results: With Choi and IU more patients were considered than PR and less than PD and SD. According to AASLD more patients were measured as SD and PD than PR. 26/40 patients were classified as PR with IU. In contrast measurements with AASLD in only 8/26 patients were also classified as PR. 6/12 SD patients measured with IU were measured as PD with AASLD. 4/26 patients classified with IU as PR were described as SD with CHOI, 10/14 SD patients measured with CHOI were SD according to IU, the other 4 patients were PR with IU. 2/4 PD patients according to CHOI were SD with IU.
Conclusion: More patients by IU were classified as SD versus PD and PR versus SD. We attribute this to the more detailed consideration of the HU differences between the virtual native and contrast-enhanced series generated by DECT. Iodine uptake (IU) in HCC measured and visualized with DECT is a promising imaging method for the assessment of treatment response after radioembolisations.
Key points: —dual energy CT of hypervascular tumors such as HCC allows to quantify contrast enhancement without native imaging.
—this can be used to evaluate the therapy response after Radioembolization.

1. Introduction

Selective internal radiation therapy (SIRT) with 90yttrium microspheres – also known as radioembolisation (RE)- is a rapidly evolving therapy option for inoperable HCC [1–6].

The response to treatment is assessed by critical clinical and laboratory parameters as well as by post- interventional cross-sectional imaging including CT or MRI. In addition to the changes in tumor size vascularization is an important marker for therapy monitoring [7–15].

In responders HCC lesions ideally show a reduction in size and decreased hyper-vascularity after RE. In some cases, a stable or even increased tumor size (so-called pseudo-progression) with reduced blood flow to the tumor mass is reported [16]. This may be attributed to tumor necrosis, hemorrhage and edema leading to increased tumor size.

Assessment of tumor response should incorporate the reduction in viable tumor burden, defined by the area (EASL) [17] or diameter (AASLD) [18] measurement of contrast enhancing tumor on arterial phase imaging to assess the tumor response. AASLD diameter measurement of viable tumor is used in clinic and considered as the standard assessment of treatment efficiency in patients receiving antiangiogenic therapy [19].

Choi et al. have proposed the measurement of CT density as a potential indicator of gastrointestinal stromal tumor (GIST) response in patients undergoing targeted therapy [20].

In rare cases, however, HCC response may result in increased density because of the intratumoral hemorrhage, which is a rare effect observed during sorafenib therapy [15], thus result mislead

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tumor density measurements and failed Choi response assessement. Therefore, ideally, new parameter directly related with neovascularisation should be acquired to assess the density differences related to contrast medium accumulation, or, those related to vital and vascularized tumor tissue [7].

Dynamic contrast-enhanced CT perfusion has been explored as potential new method for assessing response of tumor vascularization to antiangiogenic therapy but in clinic practice it is prohibited regarding the limitations (e.g. limited coverage of all tumor sites, unstandardized postprocessing, radiation dose) [21].

A recent development in CT has been the introduction of dual energy technology [22]. On such CT systems, two X-ray tubes can be operated at different tube currents, making dual energy scanning feasible. Dual energy CT implies simultaneous acquisition of data sets at two different photon spectra in a single CT examination [23] resulting in the ability to reconstruct the data at 80-kVp, 140-kVp, and weighted-average. The weighted-average data set is a combination of image data from the 80- and 140-kVp data sets and can be used to generate a virtual 120-kVp data set. In addition, virtual non-enhanced data sets can be reconstructed by using post-processing algorithms [24,25].

One important advantage of dual energy CT (DECT) when compared with a single-source system is the option to use the two tubes at different tube currents offering differentiation of materials of non-equal density. The higher the difference in the two tube currents (e.g. 80 kVp and 140 kVp) used for imaging the better is the differentiation between two materials of different density [23]. Based on these advantages potential applications of dual energy CT when evaluating the abdomen are for example [26]: Quantification and visualization of contrast enhancement, reconstruction of virtual non-enhanced images from the existing data sets obviating the need for additional non-enhanced scans. Consequently, radiation exposure for the patient may be reduced. Furthermore, calcifications may be quantified and anatomical structures of high attenuation (such as the bone) can be removed semiautomatically.

DECT) allows selective quantification and visualization of iodine-related density differences and improves the ability to detect contrast agent and to distinguish high-density substances created by iodine from those created by hemorrhage [7,21].

The aim of this prospective study was to examine the diagnostic value of iodine uptake (IU) measured with dual-energy CT (DECT) for the assessment of therapy response after RE in patients with HCC compared to measurements based on AASLD and Choi. We hypothesize that DECT may help to determine the exact contrast uptake in tumors, which could represent an important response marker in addition to changes in size.

2. Material and methods

2.1. Patient population

We prospectively analyzed data of all HCC patients who received radioembolisation and monitoring by DECT in our institution between May 2009 and January 2010. Baseline contrast enhanced DECT scan was obtained three weeks before treatment and at least one follow-up scan was obtained 12 weeks after radioembolisation. If bilobar disease was present radioembolisation treatment was staged and follow-up scan was performed 12 weeks after the last treatment.

The inclusion criteria were:

- inoperable (due to size, localization) HCC; hepatic function Child–Pugh Class A or B; presence of a measurable target lesion showing intratumoral arterial enhancement in contrast enhanced DECT [27]. The measurable diameter was at least 1 cm and the lesion was suitable for repeated measurements;
- the exclusion criteria were: prior systemic treatment; contrast allergy; renal dysfunction; hypoenhancing tumor without wash out; prior transarterial chemoembolization (TACE), or radiofrequence ablation (RFA).

Table 1
Patient demographics.

Variable	Value
Age(Years)	
mean	66.2 + - 8.3
range	52–77
Gender	
Males	24
Females	16
Etiology of liver cirrhosis	
Ethanol abuse	16
HBV	12
HCV	10
NASH	2
Child-Pugh class	
A	16
B	24
Baseline AFP	
Mean (ng/ml)	438
Range	92–4583

AFP, α-fetoprotein; HBV, hepatits B virus; HCV, hepatitis C virus; NASH, nonalcoholis steatohepatitis.

85 HCC patients were examined in our institution with DECT in this period, including 60 patients treated with radioembolisation. Finally, 40 out of 60 patients (34 men and 26 women) with 82 measurable target lesions (median 2 lesions/patient, range 1–4) were analyzed.

20 out of 60 patients were excluded from analysis 4 patients with no measurable target lesion, 16 patients with prior systemic treatment/transarterial chemoembolisation (TACE)/radiofrequence ablation (RFA).

This study was approved by our institutional review board and all patients provided written informed consent prior to their participation. Patientsí characteristics are displayed in Table 1.

2.2. DECT protocol

All CT scans were performed on a dual-source multi– detector scanner (Somatom Definition^{TM} Dual Source; Siemens Medical Solutions, Forchheim, Germany).

Patients were positioned slightly off center to the left to ensure complete coverage of the liver by the smaller field of view of detector B.

After intravenous injection of a non-ionic contrast agent (1,5 ml per kilogram of body weight, Xenetix 300^{TM}, *Guerbet, Sulzbach, Germany,* mean body weight 73 + - 17 kg, mean contrats amount 103 + - 10 ml, flow rate 4 ml/s) via an automated dual-syringe power injector (Accutron CT-D, Medtron, Saarbrücken, Germany) scanning of the arterial phase (AP) during inspiratory breath-hold was started. All patients were scanned in cranio-caudal direction from the dome of the liver to the iliac crest.

The timing for the AP scan was determined using the care bolus technique (Siemens Healthcare, Forchheim, Germany), AP scanning was automatically started 7 s after the attenuation coefficient of abdominal aortic blood reached 120 HU. The portal venous phase (PVP) images were acquired 30 s after AP.

All AP and PVP images were obtained in the dual energy (DE) mode. The DE scan was acquired with a detector collimation of