European Journal of Radiology Open 3 (2016) 162–171

Contents lists available at ScienceDirect

European Journal of Radiology Open

journal homepage: www.elsevier.com/locate/ejro

Role of dual energy spectral computed tomography in characterization of hepatocellular carcinoma: Initial experience from a tertiary liver care institute

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ARTICLE INFO

Article history:
Received 14 January 2016
Accepted 26 May 2016
Available online 20 July 2016

Keywords:
Hepatocellular carcinoma
Dual energy computed tomography
Material density images
Spectral computed tomography
Functional imaging
Iodine quantification

ABSTRACT

Objective: To investigate dual-energy spectral CT in characterization of hepatocellular Carcinoma (HCC) in patients with chronic liver disease.
Methods: Dynamic computed tomography (CT) was performed in 3600 patients (2879 males; 721 females, mean age 50.9 ± 11.9 years) with working clinical diagnosis of liver cirrhosis for hepatocellular carcinoma screening and other clinical indications. The study was conducted over a period of 3 years. During dynamic CT scanning, spectral (monochromatic) and routine (polychromatic) CT acquisitions were obtained on a single tube, dual energy, 64 slice multi-detector CT scanner. Imaging findings were studied on routine CT. On the basis of routine CT findings, indeterminate lesions (lesions not showing characteristic hypervascularity followed by washout on dynamic routine CT scan) that were referred for biopsy or surgery were segregated. A retrospective blinded review of the lesions, acquired by the spectral CT acquisitions was done with the help of gem stone imaging (GSI) software to characterize these lesions. All the above lesions were analyzed *qualitatively* in the arterial phase for lesion conspicuity as well as *quantitatively* using the monochromatic data sets and nodule Iodine concentration on material density maps, respectively. This data was studied with respect to predictability of HCC using the spectral CT technique. Iodine density of the lesion, surrounding liver parenchyma, and lesion to liver parenchyma ratio (LLR) were derived and statistically analyzed. Histopathology of the lesion in question was treated as gold standard for analysis.
Results: It was observed via statistical analysis that the value of iodine density of the lesion on material density sets of ≥29.5 mg/dl, enabled a discriminatory power of 86.5%, sensitivity of 90.5% with 95% confidence Interval (CI) (69.2–98.8%) and specificity of 81.2% with 95% Confidence Interval (54.4–95.9%) in predicting HCC. Qualitative assessment also showed higher lesion conspicuity with spectral CT image sets as compared to routine CT data.
Conclusion: This study reveals that spectral imaging is an excellent qualitative as well as a quantitative tool for assessing and predicting hepatocellular carcinoma in cirrhotic patients.

1. Introduction

The primary objective of our study was to determine whether spectral CT technique can improve accuracy in diagnosis of HCC in cirrhotic patients. This analysis was performed to evaluate both ***qualitative*** (lesion conspicuity) and ***quantitative*** (using material iodine density values) aspects of spectral CT respectively. Secondary end points and objectives of this study were to:

1. Explore spectral CT as a functional tool in patients with HCC.

Abbreviations: HCC, hepatocellular carcinoma; CT, computed tomography; GSI, gem stone imaging; DECT, dual energy computed tomography; LLR, lesion to liver parenchyma ratio; MMD, monochromatic material density; CI, confidence interval.

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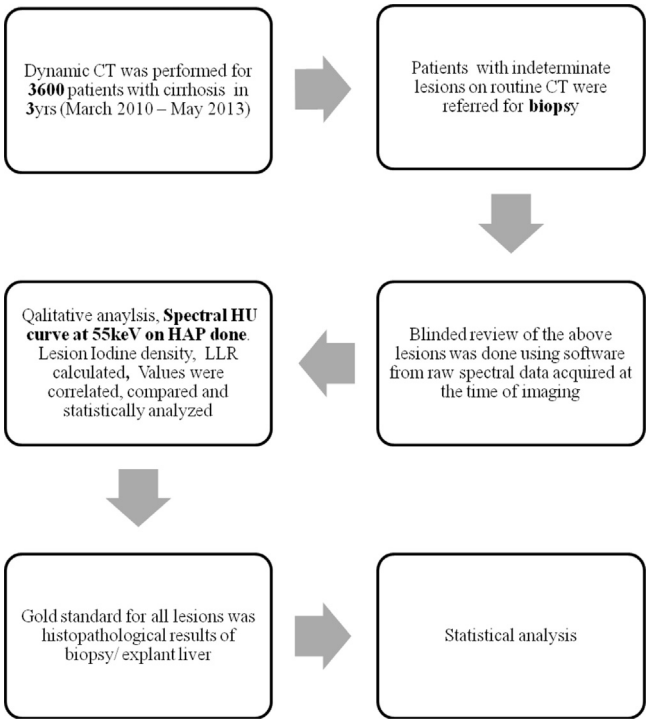
http://dx.doi.org/10.1016/j.ejro.2016.05.007
2352-0477/

2. Assess the accuracy and reliability of a new assessment parameter of measuring *iodine density* of enhancing liver nodules *on the arterial phase* of CT instead of the traditional quantification done by calculating their *attenuation values* in Hounsfield units.
3. Assign a range of iodine density values to confirmed HCC nodules so as to be able to form an objective, quantitative, value-based classification for liver cancer nodules on a future long term basis.

The revised European association of study of liver diseases (EASL) and American association of study of liver diseases (AASLD) practice guidelines on the diagnosis and management of HCC, given in 2012 and 2010 respectively, changed the way; imaging is being performed for surveillance and detection of liver lesions in patients with chronic liver disease. [1] AASLD guidelines recommend abdominal ultrasonography every 6 months for surveillance of 'at risk' population of active chronic hepatitis B, cirrhotic patients and patients in the 40–50 years bracket. [1] The EASL guidelines recommend patients with chronic hepatitis C infection and advanced stage of F3 liver fibrosis, regardless of cirrhosis, to undergo surveillance with ultrasonography. [2] The practical approach to reliability of ultrasonography to detect small lesions (< 1 cm) in a diffusely nodular liver appears questionable. For this reason, dynamic, contrast enhanced, CT is recommended to further detect and characterize such lesions. [3,4] The standard algorithm for diagnosis of HCC is the demonstration of the phenomenon of hypervascularity of a nodule or lesion in the arterial phase with subsequent hypoattenuation or "wash-out" of the lesion compared to rest of the normally enhancing liver parenchyma on the portal venous or equilibrium phase. [3–5] The challenge however; is to characterize nodules, which do not show adequate hypervascularity on the arterial phase or demonstrate inadequate "wash-out" on later phases of routine dynamic CT or MRI. These lesions are characterized as 'indeterminate' nodules on imaging and require biopsy with histopathology or further investigations (e.g. contrast enhanced sonography with kupffer cell specific contrast/MRI with SPIO or hepatocyte specific contrast) which may or may not be available at all centers. MRI is universally recognized as a problem solving modality and has a higher procedure cost with worldwide limited availability. These indeterminate/atypical tumors may be difficult to diagnose, even with all the above criteria put together. Biopsy is the current gold standard of diagnosis however; smaller lesions are technically difficult to visualize and may show lack of sufficient tissue, with nodule heterogeneity within the lesion itself. The fine needle aspiration or biopsy sample may not be representative of the entire nodule. To overcome the above lacunae, we have tried to explore spectral CT for its diagnostic capabilities in context to diagnosis of HCC, in patients with pre existing chronic liver disease, regardless of the underlying etiology. The advent of spectral CT is based on the principle that this technique involves scanning at distinctly different energies (most commonly used energy levels are 70 and 140 kVp) using a setup of *single or dual x-ray tubes* with detectors operated at two distinct energies or rapidly switching between two different energies depending on the manufacturer. [6–9] This is based on the physics principle of 'Photoelectric effect' which, is used to obtain additional information regarding tissue composition. The photoelectric effect essentially utilizes the difference in the K-edges of two elements. This principle works best for post contrast CT scans due to the use of Iodine, which has a K-edge of (33.2 keV). This K-edge is closer to lower energies (80 kVp) compared with higher energies (140 kVp) on a spectral (essentially a dual energy) CT scan and hence Iodine containing tissue is more attenuating (better visualized) at lower energies. The higher attenuation of Iodine results in improved conspicuity of ***hypervascular (Iodine rich)*** nodules in contrast to rest of the liver parenchyma.

We have tried to ascertain a baseline value of iodine material density in the arterial phase of histopathological proven cases of HCC which were labeled as "indeterminate" nodules on routine dynamic imaging. This is based on the hypothesis that we may be able to define a possible cut-off value at which we can predict the diagnosis of HCC using spectral CT alone. Our long term goal is to explore spectral CT as a functional tool using iodine density as a predictor of tissue composition and tumor grading. In future, this may obviate the need for biopsy, completely. We may be able to characterize HCC on a single-phase study, reducing radiation exposure, dosage of intravenous contrast as well as the need for second modality confirmation.

Table 1
Work flow-chart of study design and method of conducting the study.



Abbreviations: HU—Hounsfield Units; HAP—Hepatic arterial Phase; LLR—Lesion to liver parenchyma iodine density ratio.

2. Material and methods

A total of 3600 patients (mean age 50.9 ± 11.9 years, 2879 males and 721females), who were clinically proven to have liver cirrhosis due to various etiologies were scanned by routine CT (with simultaneous acquisition of spectral CT data sets) over a period of three years at our tertiary liver care hospital. All patients with liver cirrhosis, who had indeterminate liver nodules on dynamic routine CT (irrespective of the lesion size) and were, advised a histopathological analysis on imaging were enrolled in the study group. This comprised our study group of 37 patients (mean age 51.65 ± 12.33 years, 33 males and 4 females) who underwent further histopathological assessment or surgical excision of these lesions. A blinded; retrospective, double reader, single centered analysis of the spectral CT data was conducted in a clinical framework. The workflow of the study is demonstrated in a flow chart given below. (Table 1).

2.1. Inclusion criteria

'Indeterminate nodule' was defined as uncharacteristic/atypical enhancement pattern of HCC, not conforming to classical arterial hypervascularity and portal venous or equilibrium phase washout on dynamic scans.