ROLE OF MULTI-DETECTORS COMPUTED TOMOGRAPHY PERFUSION (MDCT-P) IN DIFFERENTIATING HEPATOCELLULAR CARCINOMA FROM HEMANGIOMAS

Hosam Mostafa Kamel1 and Ahmed Qasem Mohammed2

Diagnostic Radiology Department, South Egypt Cancer Institute, Assuit University1 and Department of Tropical Medicine, Gastroenterology and Hepatology, Alazhar University Assuit2, Egypt.

ABSTRACT

**Aim:** To determine the role of multi-detectors CT perfusion in differentiating hepatocellular carcinoma from hemangiomas. **Material and Methods:** This prospective study included 42 patients underwent multi-detectors computed tomography perfusion (MDCT-P) with detected hepatic focal lesions by MDCT. They are divided into 2 groups: Group I Hepatocellular carcinoma (22 cases, 13 males and 9 females), Group II Hemangiomas (20 patients, 2 males and 18 females). **Results:** In group I (Hepatocellular carcinoma) the BF show significant increase (near four times) (mean: 281.9 mm/min/100g) compared with the BF of background liver (72.8 mm/min/100g) with significant P value (0.009). While MTT show significant decrease in HCC (mean was 8.7 sec.) in compared with liver which was (21.5 sec) with 0.001 P value. The PS and BV show no significant changes. In group II (Hemangioma) significant reduction in BV compared with the background liver with significant P value (0.02), changes in BF, MTT and PS of examined Hemangiomas compared with normal liver parenchyma have non-significant P value more than 0.05 denoting non-significant relations between these results. **Conclusion:** Perfusion CT is a helpful tool in differentiating hepatocellular carcinoma from hemangiomas by its ability to determine changes in perfusion parameters of the lesions.

INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common primary hepatic tumor and one of the most common cancers worldwide (1). HCC is a primary malignant tumor of hepatocellular origin that develops in patients with risk factors such as alcohol abuse, viral hepatitis and metabolic liver disease. It can also occur, rarely, in patients with normal liver parenchyma. Grossly, HCC can undergo hemorrhage and necrosis because of a lack of fibrous stroma. Vascular invasion, particularly of the portal system, is common. Invasion of the biliary system is less common. Aggressive HCC can cause hepatic rupture and hemoperitoneum. There are 3 growth patterns exhibited by HCC: solitary mass often large, multifocal or nodular pattern multiple nodules and diffuse multiple small foci scattered diffusely throughout the liver (1).

Tumors that are more differentiated can produce bile. HCC can produce alpha-fetoprotein (AFP) as well as other serum proteins. However, this is an insensitive parameter because AFP levels may be normal in more than one third of patients (2).

Tumor angiogenesis is essential for cancer growth and provides an attractive target for oncologic therapies. CT perfusion is an emerging imaging tool that provides both qualitative and quantitative information regarding tumor angiogenesis (3). With the introduction of multi-detectors CT scanners, it is now possible to cover up to 16 cm in one rotation, and thereby making it possible to scan entire organs such as the liver with a fixed table position.

AIM OF WORK

This study aimed to determine the role of computed tomography perfusion in differentiating hepatocellular carcinoma from hemangiomas.

PATIENTS AND METHODS

Study duration:
This is a prospective study, which was carried out during the period between September 2013 and September 2015.

Study place:
This study was carried out at Radiology Department of South Egypt Cancer Institute (Asyut University).

Inclusion Criteria:
1. Both sexes of different age groups were included.
2. Patients who have hepatic focal lesions detected by abdominal ultrasound and/or triphasic MDCT suspected to be hepatocellular carcinoma or hemangioma, these patients are underwent MDCT liver perfusion before the further confirmatory methods either by biopsy or follow up.

Exclusion Criteria:
1. Hypersensitivity to the dye
2. Renal impairment.
3. Pregnant females.

**Patient preparation:**
-Detailed Clinical history assessment to exclude any contraindications to contrast media.
- Laboratory data: Particular interest in the results of the renal function tests (creatinine level < 1.4 mg/dL).
- Informed consent was required before study participation.
- Venous access: An 18-gauge cannula was placed into a superficial vein within the antecubital fossa. Injection was done via automatic power injector.
- Patient’s position: Patient was positioned supine on the CT table in the “head first” position with his arms resting comfortably above the head.

Technique of examinations:
CT scanner: CT perfusion was done using a 16 multi-detectors CT scanner (GE BrightSpeed16).
Pre-contrast series: One abdominal scout was acquired in antero-posterior view then pre-contrast axial cuts were taken during a breath hold at the end of inspiration. The coverage area starts from the level of the top of the right diaphragmatic copula (Hepatic Dome) till 20 cm caudally (end of iliac crest).
CT perfusion: After tumor localization, a 2-cm region was selected (because we use 16 multi-detectors CT provide only 2cm coverage for perfusion scan) based on the pre-contrast series for the dynamic study.
A dynamic study of the selected area was performed in a single breath hold at the end of inspiration at a static table position.
A total of 50 mL of nonionic iohexol contrast medium: (Omnipaque350 mg of iodine/mL; GE- Gantry rotation time = 1 second.
- 100 kvp, 240 mA.
- Acquisition in 4i transverse mode (four sections per gantry rotation) and 5-mm reconstructed section thickness.
- Scanning was initiated after a 5-second delay from the start of injection and images were acquired for a total duration of 60 seconds.

Data Analysis:
- Data were processed at a workstation (Advantage Windows 4.0: GE Medical Systems) with CT perfusion software (GE Perfusion 4).
- Functional data were calculated by the following steps:
  - Displaying images at an appropriate window, such as soft tissue for abdomen (width =400 HU, level = 40 HU).
  - Obtaining a reference portal input curve by placing a region of interest (ROI) in the aorta manually ensuring that the ROI did not include any mural calcification.
  - Obtaining a reference arterial input curve by placing a region of interest (ROI) in the main PV, portal vein branch, superior mesenteric vein (SMV), splenic vein (SV).
  - Then perfusion maps and values are computed.
  - ROI was drawn in background liver parenchyma.
  - ROIs for tumor were hand drawn, in the presence of multiple tumors: ROIs were drawn for all tumors in the scanning range.
  - Perfusion values of tumor(s), background liver was then calculated averaging the functional parameters across all four sections and displayed as:
    - Tables of multiple parameters such as BF, BV, MTT, PS and HAF values.
Health Care) was injected at a rate of 5 mL/sec. The following CT parameters were used to acquire dynamic data:
These parameters can be defined as the following:
1) Blood flow (BF): This is the volume flow rate of blood through the vasculature in a tumor. It is expressed in units of ml/min/100g.
2) Blood volume (BV): This is the volume of blood within the vasculature in a tumor that is actually ‘flowing’. Any stagnant pool of blood will not be included in the blood volume. It is measured in units of ml/100g.
3) Mean transit time (MTT): This is the average time taken by blood elements to traverse the vasculature from the arterial end to the venous end in a tumor. Mean transit time is measured in seconds.
4) Capillary permeability surface area product (PS): it is the unidirectional flux of contrast from blood plasma to interstitial space. It is measured in units of ml/min/100g.
5) Hepatic Arterial Fraction (HAF): Percentage total blood flow of the tumor that is originated from hepatic artery.

Functional maps of BF, BV, MTT and PS. These functional maps were displayed in colors ranging from blue to red, blue being the lower range of display for BF, BV, and PS and red being the upper range of display.

Statistical methods:
IBM SPSS statistics (V.20, IBM Corp., USA, 2010) was used for data analysis. Data were expressed as Mean ± SD for quantitative parametric measures and as Median Percentiles for quantitative non-parametric measures.

The following tests were done:
1. Comparison between two independent groups for non-parametric data using Wilcoxon Rank Sum test.
2. Ranked Sperman correlation test to study the possible association between each two variables among each group for non-parametric data. The probability of error at 0.05 was considered significant while at 0.01 and 0.001 are highly significant.

3. Diagnostic validity test: It includes:
   a. The diagnostic sensitivity (Sn.): It is the percentage of diseased cases truly diagnosed (TP) among total diseased cases (TP+FN).
   b. The diagnostic specificity (Sp.): It is the percentage of non-diseased truly excluded by the test (TN) among total non-diseased cases (TN+FP).
   c. The predictive value for a +ve test (P+): It is the percentage of cases truly diagnosed among total positive cases.
   d. The predictive value for a -ve test (P-): It is the percentage of cases truly negative among total negative cases.
   e. The efficacy or the diagnostic accuracy of the test (Eff.): It is the percentage of cases truly diseased plus truly non-diseased among total cases.

4. The receiver operating characteristic (ROC) curve was constructed for some parameters:
   - **Purpose:** to obtain the most discriminating parameters between the compared groups.
   - **Method:** The true positive rate (Sensitivity) is plotted in function of the false positive rate (100-Specificity) for different cut-off points of a parameter.
   - The area under the curve (AUC) can be then calculated. AUC is a measure of how well a parameter can distinguish between two groups.
RESULTS
This study includes 42 patients, diagnosed to have hepatic focal lesions by triphasic MDCT then further evaluations (laboratory and biopsy) were done to fulfill its final diagnosis as previously mentioned. 15 were males and 27 were females. Their age range from 20-68 years. Each patient underwent liver perfusion study, the resulting perfusion parameters (BV, BF, MTT, PS, and HAF) were used by IBM SPSS statistics for data analysis. They are divided into 2 groups:

Group I:
- 22 patients were newly diagnosed as hepatocellular carcinoma before any therapeutic procedure (13 males and 9 females).

Clinical data:
60 years old male patient, presented with two HFLs on top of cirrhotic liver with raised alpha fetoprotein.

![Arterial phase](image1)
![Portal phase](image2)
![CT perfusion maps](image3)

Figer 1: Arterial phase (A) Show two hypodense focal lesions seen in segments V, VI and VII and segment III and both show early arterial enhancement, Portal phase (B) show early wash out of both focal lesions, CT perfusion (C & D) show ROI 1 in Aorta, ROI 2 in PV, ROI 3 in normal left hepatic lobe, ROI 4 and 7 in left hepatic small focal lesion and ROI 5 & 6 in right hepatic focal lesion. CT perfusion maps (E, F, G, H and I) show increased BF of hepatic focal lesion and decrease MTT of hepatic focal lesion compared with liver parenchyma.

Table (1): CT perfusion parameters of normal liver parenchyma (ROI 3) and left hepatic focal lesion (ROI 4 and 7) and right hepatic focal lesions (ROI 5 and 6).
Table (2): Perfusion parameters of background liver and HFLs:

<table>
<thead>
<tr>
<th>ROI</th>
<th>Perfusion parameters</th>
<th>BV</th>
<th>BF</th>
<th>MTT</th>
<th>PS</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROI 3</td>
<td>background liver</td>
<td>31.83</td>
<td>162.9</td>
<td>15.76</td>
<td>39.3</td>
</tr>
<tr>
<td>ROI 4</td>
<td>4Lt HFL</td>
<td>32.86</td>
<td>264.3</td>
<td>15.96</td>
<td>44.95</td>
</tr>
<tr>
<td>ROI 5</td>
<td>7 Lt HFL</td>
<td>39</td>
<td>417.6</td>
<td>11.57</td>
<td>30.95</td>
</tr>
<tr>
<td>ROI 6</td>
<td>5 Rt HFL</td>
<td>18.45</td>
<td>354.8</td>
<td>5.395</td>
<td>1.329</td>
</tr>
<tr>
<td>ROI 7</td>
<td>6 Rt HFL</td>
<td>15.54</td>
<td>206.9</td>
<td>4.618</td>
<td>1.233</td>
</tr>
</tbody>
</table>

Noted increase in BF and decrease in MTT of the HFL compared with background liver, which is matching with malignancy, with noted decrease in the PS and BV of large right hepatic focal lesion but PS and BV of small focal lesion show no significant changes.

Diagnosis:
Tri-phasic MDCT was typical for HCC with elevated alpha fetoprotein and cirrhosis. CT perfusion was matching with malignancy due to (increase BF and decrease MTT), biopsy proved HCC.

Group II:
• 20 patients were hemangiomas. Two males and 18 females. Based on typical triphasic CT criteria, 12 cases underwent additional MRI, while four cases diagnosed by biopsy (fig. 2).
Fig. 2 (A-G): Female patient 60 years, with single HFL, Triphasic MDCT shows absence of intratumoral enhancement and only peripheral puddles of enhancement (isodense to aorta) in the arterial phase (A), followed by peripheral nodular enhancement in the portal phase (B) with still persistent enhancement of the lesion on delayed venous phase (C). Axial perfusion scan with multiple ROIs (D). Perfusion maps (E-F) and perfusion parameters of background liver ROI 3 and HFL ROI 4 (G) shows decrease in BV, BF, with no significant changes in the MTT. The decrease in BV and BF behave the benign nature. MDCT was suggestive of hemangioma, which is proved by biopsy.

Regarding Hepatocellular carcinoma lesions
Among the examined HCC cases, there is significant changes in certain perfusion parameters of the tumor compared with those measured in the background liver of the same patients. These changes and their percentage can be summarized in the following table:

Table (3): Changes in perfusion parameters among HCC with their percentage.

<table>
<thead>
<tr>
<th></th>
<th>Increase</th>
<th></th>
<th></th>
<th></th>
<th>Decrease</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BV</td>
<td>14</td>
<td>63.3</td>
<td>8</td>
<td>36.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BF</td>
<td>22</td>
<td>100.0</td>
<td>0</td>
<td>0.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MTT</td>
<td>0</td>
<td>0</td>
<td>22</td>
<td>100</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PS</td>
<td>16</td>
<td>72.7</td>
<td>6</td>
<td>17.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
<td>63.3</td>
<td>8</td>
<td>36.4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The resulting changes can be described as the following:
• BF show increase in 100% of cases.
• MTT show decrease in 100% of cases.
• BV and PS show increase in 63.3% and 72.2% of cases respectively.

Comparison between each perfusion parameter of the HCC and of the background liver is illustrated in the following table:

Table (4): Comparisons between perfusion parameters of focal lesions and background liver in HCC patients:

<table>
<thead>
<tr>
<th></th>
<th>Background liver</th>
<th>HCC</th>
<th>R</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean</td>
<td>Standard deviation</td>
<td>mean</td>
<td>Standard deviation</td>
<td></td>
</tr>
<tr>
<td>BV</td>
<td>29.5</td>
<td>7.7</td>
<td>21.2</td>
<td>17.6</td>
</tr>
<tr>
<td>BF</td>
<td>72.8</td>
<td>13.8</td>
<td>281.9</td>
<td>221.5</td>
</tr>
<tr>
<td>MTT</td>
<td>21.5</td>
<td>2.5</td>
<td>8.7</td>
<td>4.6</td>
</tr>
<tr>
<td>PS</td>
<td>8.2</td>
<td>5.1</td>
<td>10.8</td>
<td>12.6</td>
</tr>
</tbody>
</table>

The previous table show:
• Noted significant increase (near four times) in mean BF of HCC (281.9 mm/min/100g) compared with BF of the background liver (72.8mm/min/100g), with P value 0.009.
• While MTT show decrease in the HCC compared with background normal liver (mean was 8.7 seconds in HCC and 21.5 sec. in background liver), with P value 0.001.
• On the other cut off values have no significant P value in BV and PS.

(Fig: 3) Graph show the relation between the BF of HCC (green) and background liver (blue)

(Fig: 4) Graph show the relation between the BV of HCC (green) and background liver (blue).

(Fig: 5) Graph show the relation between the MTT of HCC (green) and background liver
(Fig: 6) Graph show the relation between the PS of HCC (green) and background liver(blue).

Regarding group II (Hemangiomas) comparison between their perfusion parameters and those of background liver is done (table 5).

**Table (5): Changes between liver and benign lesions and their significant:**

<table>
<thead>
<tr>
<th></th>
<th>Background liver</th>
<th>Hemangiomas</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>BV</td>
<td>39.2</td>
<td>31.8</td>
</tr>
<tr>
<td>BF</td>
<td>105.8</td>
<td>91.4</td>
</tr>
<tr>
<td>MTT</td>
<td>19.8</td>
<td>9.6</td>
</tr>
<tr>
<td>PS</td>
<td>9.4</td>
<td>9.4</td>
</tr>
</tbody>
</table>

From the previous table, it's noted that:

- BV show decrease in Hemangiomas compared with the background liver.
- Changes in BF, MTT and PS of examined Hemangiomas compared with normal liver parenchyma have non-significant, P value more than 0.05 denoting non-significant relations between these results (fig. 7).

(Fig: 7) Graph show the different between the BV in background liver (blue) and the hemangiomas (green).

The following table show parameters cut off between hepatocellular carcinoma and the benign, with their accuracy (table 6 and fig.8&9).
Table (6): Cut off between HCC and Hemangiomas and their accuracy.

<table>
<thead>
<tr>
<th></th>
<th>Hemangiomas</th>
<th>HCC</th>
<th>Cut off</th>
<th>accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>min</td>
<td>max</td>
<td>Median</td>
<td>min</td>
</tr>
<tr>
<td>BV</td>
<td>0.9</td>
<td>30</td>
<td>9.2</td>
<td>4.6</td>
</tr>
<tr>
<td>BF</td>
<td>47</td>
<td>337</td>
<td>63</td>
<td>103</td>
</tr>
<tr>
<td>MTT</td>
<td>2.5</td>
<td>14</td>
<td>10</td>
<td>1.1</td>
</tr>
<tr>
<td>HAF</td>
<td>0.4</td>
<td>0.6</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>PS</td>
<td>4.1</td>
<td>25</td>
<td>8.7</td>
<td>1.4</td>
</tr>
</tbody>
</table>

The previous table show the median of each parameter, the cut off values between HCC and Hemangiomas with their accuracy, which can be summarized as the following:

- BF show significant increase in HCC compared with those of Hemangiomas with cut off (63mm/min/100g) and 92% accuracy.
- BV show also increase in HCC with (9.2mm100g) and 75% accuracy.
- MTT show also decrease in HCC with(4.4 mm100g) and 92% accuracy.
- PS show increase in HCC with 78% accuracy of cut off.

(Fig: 8) Graph show the relation between BF in the Hemangiomas (blue) and HCC (green).

(Fig: 9) Graph show the relation between MTT in Hemangiomas (blue) and HCC (green).
DISCUSSION
Accurate detection and evaluation of focal liver lesions (FLLs) are important for treatment planning in patients with liver neoplasm such as hepatocellular carcinoma (HCC) (4).
CT perfusion is an emerging imaging tool that provides both qualitative and quantitative information regarding tumor angiogenesis by measurement of regional blood flow (BF), blood volume (BV), and vessel permeability using dynamic contrastenhanced imaging techniques including CT perfusion( 5)
The overall number of patients is 42 patients: 22 were newly diagnosed as hepatocellular carcinoma and 20 patients were hemangiomas.

Regarding HCC cases :
HCC patients: diagnosed by either triphasic CT criteria (arterial enhancement, following by contrast washout in subsequent phases), associated with cirrhotic background liver and a high alpha fetoprotein, which is matching the non invasive diagnostic criteria for HCC reported by Josep and Michel 2011 (6), however only two cases in the study proved by biopsy.

Then perfusion maps are formed and quantitative assessment of HCC perfusion parameters are measured. Then we compared them to the background liver parameters, which are blood flow (BF), blood volume (BV), mean transit time (MTT), and permeability-surface area product (PS). The comparison revealed:

• BF show increase in 100% of HCC cases with significant increase (near four times) with mean (281.9 mm/ min/ 100g) compared with BF of the background liver (72.8mm/min/100g), with P value 0.009.
• MTT show decrease in 100% of cases (mean was 8.7 seconds in HCC and 21.5 sec. in background liver), with P value 0.001.
• BV and PS show increase in 63.3% and 72.2% of cases respectively, but with no significant P value of their cut off values.

Similar findings were found by Zhong et al 2009(7) who reported higher BF in primary hepatic carcinoma when compared to background liver and were found also by Komemushi et al 2005(8) who obtained the pure arterial perfusion of HCC by CT hepatic arteriography, and found significant increase of arterial BF and BV in tumors. Wang et al 2011 (9) he also found relative increase of BF and BV among HCC lesions when compared to background liver.

The high BF and BV among HCC lesions can be explained by the process of angiogenesis, which is based on the activation, proliferation and migration of endothelial cells induced by secreted angiogenic factors. This process leads to formation of network of numerous vessels which have irregular diameters and abnormal branching pattern. On the other hand, the high PS among HCC lesions can be explained by the fact that HCC blood vessels are leaky as they lack a complete basal membrane, and are incompletely covered by pericytes(10).

MTT show decrease in the HCC comparing this with the adjacent liver. This is consistent with Guo Ma, et al .2012 (11) as they found that decrease the MTT is one of the early hemodynamic changes in HCC. This may be explained by the fact that the formation of new arterial vessels per unit mass determines a corresponding reduction in time of blood passage from arterial to venous end per second.

However in our study no significant increase in the BV that’s may be due to variable degree of fibrosis and cirrhosis of the background liver of examined cases, and this may alter different liver perfusion parameters from stage to another which is proved by Ronot et al .2010(12) and so it may disturb the relative relation of BV between HCC and background liver (however BF relative changes not well affected as it show considerable four times increase in HCC compared with background liver, in contrast to BV which show only small increase which can be easily affected by any changes of total liver perfusion either arterial or portal.

These results agree with Dushyant et al .2007 (13) who found that HCC show higher BF, BV, and PS values and a lower MTT. The BF in their study was 132.3 mL/100 g/min, BV of 5.8 mL/100 g, MTT of 4.4 and seconds, and PS of 32.5 mL/100 g/min, respectively. Our results are show higher figures this may due to more fibrosis in our cases which already elevate the BV, BF, PS and elongate the MTT and so our figures are higher.

Regarding hemangiomas:
Among the whole examined hemangiomas (20) we found that BV show significant decrease in hemangiomas compared with the normal liver however changes in BF, MTT and PS of examined focal lesions compared with normal liver parenchyma have non significant P value more than 0.05 denoting non significant relations between these results.
Similarly Zagoria 2004(14) prove that Hemangiomata showed predominantly low BF, BV, PS which can be explained based on the histopathology of these tumors which are predominantly composed of endothelium-lined
vascular spaces that are perfused by slowflowing blood to the extent that Thrombosis may occur as a result of the relatively static blood flow causing relatively low values of BF and BV among these tumors. However our study failed to prove significant results among these cases in BF and PS this may due to small number of cases in our study.

One of the most important goals of the current study was to demonstrate the potential ability of the CT perfusion parameters to differentiate between each study groups. This would have great clinical applications .And so among the whole examined cases, the perfusion parameters of each group were compared with each other to reach significant cut off between them.

**COMPARISON BETWEEN HCC AND HEMANGIOMAS REVEALED**

BF and MTT showed more diagnostic validity than BV and PS

- BF show significant increase in HCC compared with those of hemangiomas with cut off ( 63mm/min/100g) and 92% accuracy.
- MTT show also decrease in HCC with (4.4 mm100g) and 92% accuracy
- BV and PS show decrease in HCC with but lower accuracy of cut off.

Our study results coincide with the results of Barnes 2010(15) who studied 11 hepatocellular carcinoma lesions and 15 hepatic cavernous hemangiomas. He found that BF and BV were significantly higher in the hepatocellular carcinoma group compared to those with hemangioma. It is also consistent with Eric 2010 (16) who confirms that MTT were significantly shorter in the hepatocellular carcinoma group compared to patients with hemangioma.

**CONCLUSION**

Perfusion CT is a helpful tool in differentiating Hepatocellular carcinoma (HCC) from hemangiomas by its ability to determine changes in perfusion parameters of the lesions.

**LIMITATIONS OF THE STUDY**

The current study faced some difficulties such as the small coverage volume of the CT perfusion (due to using 16 MDCT) which is not supposed to be a problem in largest number especially the recently introduced up to 256-detector row multi-slice CT scanners. We recommend further studies using such new CT machines to test the potential ability of CT perfusion in detection of hepatocellular carcinoma.

**REFERENCES**


11- Guo-Lin Ma, Rong-Jie Bai, Hui-Jie Jiang, Xue-JiaHao, Xu-Peng Dong, Da-Qing Li, Xin-Ding Liu and Lai Wei .Early changes of hepatic hemodynamicsmeasured by functional CT perfusion ina rabbit model of
liver tumor

12- Ronot , Tarik Asselah , Valérie Paradis , Nicolas Michoux , Mylène Dorvillius , Gabriel Baron , Patrick Marcellin , Bernard E. Van Beers Valérie Vilgrain.

13- Dushyant V. Sahani Anagaraj, Setty Holalkere, Peter R. Mueller Andrew X. Zhu, vanced.


16- Eric Barnes. CT perfusion distinguishes HCC from other liver lesions, AuntMinnie.com staff writer, April 29, 2010.