Evaluation of hepatocellular carcinoma (HCC) with multidetector row helical computed tomography (MDCT): the presence of the feeding artery correlates with the presence of pseudocapsule.

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Purpose

Hepatocellular carcinoma (HCC) is the sixth most common cancer in the world and the third in cancer related deaths after lung and gastric [J Ferlay et al, Globocan 2008]. HCC is the most frequent liver neoplasm; its incidence is increasing worldwide due to expansion of hepatitis C virus infection and NASH (non alcoholic steato hepatitis). At 2006, more than 40.000 europeans died due to HCC. This tumor receives its blood supply from the hepatic arterial vessels. By contrast, normal liver tissue receives more than 70% of its bloody supply from the portal vein. This specific characteristic is mainly used in diagnosis and also in the intra-arterial treatments of HCC (both TACE and radioembolization with Yttrium$^{90}$). Non invasive diagnostic criteria based on imaging characteristics have been recently updated [Bruix&Sherman, AASLD 2010]: uptake of contrast in arterial phase followed by rapid washout in portal/delayed phases. To our knowledge, it has not been well established the effectiveness of MDCT angiography in the identification the feeding artery (FA) of HCC. In this study, we will analyze the sensitivity of the MDCT to detect the FA of HCC and its correlation with tumor size and other radiographic findings: tumor enhancement pattern and presence of pseudocapsule.
Methods and Materials

PATIENTS

We have reviewed 53 HCC nodules in 33 cirrhotic patients diagnosed at our institution between January 2009 and June 2010.

Inclusion criteria were:

- Histological confirmation (biopsy, surgery)
- Three-phase dynamic liver study with MDCT scan, according to the protocol established in our hospital, as part of the diagnosis and/or staging of the tumor.
- No prior treatment.

By definition, in those surgical specimens, (both explants of liver transplantation and those derived from surgical resection), all tumors detected at the MDCT scan were considered compatible with HCC if they were larger than 10 mm and were HCC according to pathological report (International Working Party classification). In multifocal disease, all nodules larger than 10 mm in diameter with similar enhancement pattern as the biopsy-proved HCC nodule were considered also HCC by MDCT scan.

The nodules were stratified according to the maximum diameter of the lesion into three groups: 10 - 19mm, 20-29mm and # 30mm.

IMAGING ACQUISITION: After signed informed consent, all patients underwent a liver dynamic three-phase by using 64- multi-detector row helical scanner (MDCT) (Toshiba Aquilion). The scanning parameters: tube voltage 120kV, 180-400mA intensity modulated dose, slice thickness 1mm, reconstruction interval 5mm. Each acquisition was obtained in a cranio-caudal direction without gantry angulation and during a single breath hold.

A total of 125 ml of nonionic contrast material (Ioversol, Optiray Ultrayet® 320mg I / ml) was injected into an antecubital vein by means of a power injector (Optivantage®DH, Tyco, Mallin CKRODT) at a rate of 4ml/seg , flushed with 20 mL of 0.9% saline.

The liver dynamic study consisted of three phases: arterial, portal and equilibrium. The start time for the hepatic arterial phase acquisition began automatically by adding 8 sec to the time of peak aortic enhancement after achievement of 150-UH attenuation of the descending aorta measured with a bolus tracking technique. The ensuing average start time for the hepatic arterial phase was 27 sec (range, 25-29 seconds). The portal phase
was acquired at 70 seconds after the start of contrast material and equilibrium phase at 240 seconds.

**IMAGE ANALYSIS:** All images were analyzed independently by two radiologists on a Workstation Vitrea® 2 version 4.1.2.0 and evaluated using axial and multiplanar reconstructions by means of MIP and VR.

Image analysis had two steps: qualitative analysis and supplementary quantitative analysis.

- **Qualitative:** This analysis includes:
  
  - **The arterial supply** was evaluated during the arterial phase of dynamic study. The finding was considered positive if one or more arteries reached the periphery of the tumor, whether intra or extrahepatic origin (Fig. 1 on page 6).
  
  - **The enhancement pattern of nodules** in the three phases of dynamic study. The attenuation of HCC was classified as hyperattenuation, isoattenuation or hypoattenuation, compared with the surrounding liver parenchyma on arterial, portal and equilibrium phases. The typical HCC pattern was defined according to HCC guidelines, as seen above: hyperenhancement on arterial phase followed by washout in portal and delayed phases. The term washout was defined as occurring when any part of the lesion that was hiperattenuating on arterial phase had a corresponding hipoattenuating area relative to the adjacent liver parenchyma on portal venous phase or equilibrium phase images (Fig. 2 on page 6) The other nodules classified as HCC according to histology that not present this pattern of enhancement were defined as atypical. If it was difficult to determine tumor attennuation by visual inspection, the result of quantitative analysis of HCC were used as a reference.
  
  - **The presence of pseudocapsule** was defined as a thin and continuous ring of high uptake of contrast in the portal or equilibrium phase (Fig. 3 on page 7).

  - **Quantitative analysis:** The lesions were objectively assessed by using a circular region of interest (ROI). The mean attenuation value within the tumor and the normal liver parenchyma adjacent to the tumor was measured in Hounsfield units (HU) in order to calculate the attenuation differences between them, in the three phases of the study.

  When the difference between the attenuation of the tumor and the surrounding liver tissue was higher than 10 Hounsfield Units (HU), it was considered significant and the nodules were defined as hyperdense (Fig. 4 on page 8) or hypodense (Fig. 5 on page 9) according to this criteria. If this difference was lower than 10 HU, the nodule was defined as isodense.
STATISTICAL ANALYSIS OF DATA:
• Continuous variables were described using mean and standard deviations.
• Nominal variables were described by relative and absolute frequencies.
• To check the relationship between nominal variables we used the Chi square test. To assess the equality of means between two groups, we used the Student t test with Welch correction.
• We checked the normality of the variables by Kolmogorov-Smirnov test.
• All statistical tests were 2-sided, and a significant difference was considered when p<0.05.
Fig. 0: Footnote: Arterial phase of MDCT scan study showing a large HCC located in the right liver lobe with at least two feeding arteries (arrows).

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**Fig. 0**: Footnote: HCC with typical enhancement pattern in all three phases of the dynamic study: hyperenhancement in the arterial phase followed by washout in the portal and equilibrium phases.

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Fig. 0: Footnote: Portal phase of the dynamic study: HCC located in the right liver lobe with pseudocapsule (arrow).

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Fig. 0: Footnote: Hyperdense lesion example: Images in arterial phase. ROI measurements were obtained from the tumor (yellow arrow) and the adjacent hepatic parenchyma (blue arrow).

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Fig. 0: Footnote: Hypodense lesion example: Images in delayed phase. ROI measurements were obtained from the tumor (yellow arrow) and the adjacent hepatic parenchyma (blue arrow).

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Results

Of the 33 patients, 31 were men (93%). Mean age was 62 ± 10 years (age range, 47 -78 years).

The most common etiology of underlying liver disease was alcohol (8) and hepatitis C virus infection (15), either alone (8) or in combination with hepatitis B virus (2), or alcohol (5) (Fig. 1 on page 12).

The histological diagnosis of HCC was established by liver biopsy in 17 patients, after surgical resection in 7 and by examination of liver explants in 7.

Of the 33 patients, 20 had a nodule, 8 had 2, 3 had 3 and 2 had 4 nodules that met the criteria for inclusion in the study.

Size distribution was as follows: 16<19mm, 14<29mm, 23≥30mm (Fig. 2 on page 12).

FA was identified in 33, more frequently in nodules≥30 mm, OR=63(95%CI 6.3-630), p<0.0001. (Fig. 3 on page 13)

There were no difference between pattern of HCC and identification of FA (p=0.121). (Fig.4 on page 14)

There was relationship between pseudocapsule and FA, OR=5.6 (95%CI 1.6-19), p=0.0043. (Fig. 5 on page 15)

Six of 18 nodules with atypical pattern of enhancement presented with both pseudocapsule and FA (Fig 6 on page 16)
**Fig. 0:** The underlying etiology of cirrhosis

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<table>
<thead>
<tr>
<th>Size (mm)</th>
<th>Nodules</th>
<th>%</th>
<th>Mean± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-19</td>
<td>16</td>
<td>30.1</td>
<td>13.8±2.5</td>
</tr>
<tr>
<td>20-29</td>
<td>14</td>
<td>26.4</td>
<td>24.3±2.7</td>
</tr>
<tr>
<td>≥30</td>
<td>23</td>
<td>43.3</td>
<td>60.6±37</td>
</tr>
</tbody>
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**Fig. 0:** Distribution of nodules according to size

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**Fig. 0:** Number of nodules according to the size with/without feeding artery.

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**Fig. 0:** Number of nodules according to the pattern of enhancement, in which the arterial supply is identified.

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**Fig. 0:** Number of nodules according to the presence or absence of feeding artery (FA) with/without pseudocapsule.

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**Fig. 0:** Number of nodules with atypical pattern of enhancement according to the presence or absence of feeding artery (FA) and with/without pseudocapsule.

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Conclusion

1. The sensitivity of MDCT scan to detect the feeding artery was of 62.26%. This hazard was related to the tumor size.

2. The presence of feeding artery correlates with the presence of pseudocapsule, but its relationship with the presence of typical enhancement pattern of HCC was not statistically significant.

3. Both characteristics, the presence of feeding artery and the existency of pseudocapsule, depicted by MDCT, are present in 30% of atypical HCC nodules and they could be useful in non-invasive diagnosis of HCC. Further studies are warranted.
References


Personal Information