Evaluation of hepatocellular carcinoma with computed tomography perfusion imaging

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Aim: To evaluate the role of computed tomography (CT) perfusion imaging in patients with hepatocellular carcinoma (HCC).

Materials and methods: Seventeen patients (9 men, 8 women) with newly diagnosed HCC, proven by biopsy, were evaluated with 256-slice helical CT. Perfusion parameters of blood flow (BF), blood volume (BV), arterial perfusion (AP), portal perfusion (PP), and hepatic perfusion index (HPI) were calculated in the normal liver parenchyma and HCC samples.

Results: A total of 21 histologically proven HCC lesions were evaluated from CT perfusion images. BF, BV, AP, and HPI values were shown to be significantly higher (P < 0.05) in the HCC lesions than in the normal liver parenchyma. Conversely, PP values were found to be significantly lower (P < 0.05) in HCC relative to liver parenchyma.

Conclusion: CT perfusion imaging has the ability to evaluate tumor assessment, characterization, and neoangiogenesis in HCC.

Key words: Computed perfusion imaging, hepatocellular carcinoma

1. Introduction
Hepatocellular carcinoma (HCC) is the fifth most common malignancy worldwide, with a very high mortality (1). Only 20% of patients are suitable for curative resection at the time of diagnosis (2). HCCs are highly vascular and the status of angiogenesis correlates with the disease progression and prognosis. Therefore, assessment of tumor vascularity is important for determining the course of the disease and the response to treatment. Functional computed tomography with perfusion imaging (CT perfusion imaging) is a noninvasive technique that provides a quantitative assessment of tumor vascularity using various parameters. The aim of our study was to evaluate the role of CT perfusion imaging in patients with HCC.

2. Materials and methods
2.1. Patients
We included in our prospective study 18 consecutive patients with newly diagnosed HCC, proven by biopsy. Subjects who had clinical evidence of liver and/or renal and/or cardiac failure, history of hypersensitivity to iodinated contrast agents, or acute/chronic portal vein thrombosis were excluded. The final study group consisted of 17 patients (9 men, 8 women; mean age: 58 ± 6 years, range: 47–72 years). In this group, 14 patients had a solitary tumor, 2 patients had 2 tumors, and 1 patient had 3 tumors. This prospective study was approved by our institutional review board and written informed consent was obtained before CT perfusion imaging.

2.2. CT perfusion imaging
Multidetector CT perfusion imaging was performed in 17 patients with 256-slice helical CT (SOMATOM Definition Flash CT, Siemens Medical Solutions, Erlangen, Germany). Before CT scanning, the medial cubital vein or basilic vein of each patient was catheterized with an 18-gauge cannula for the administration of a contrast agent. An unenhanced scan was obtained first. Each subject was intravenously injected with 50 mL of contrast material (Omnipaque 350, Amersham Health, Cork, Ireland) with a flow rate of 5 mL/s followed by 60 mL of saline flush at 5 mL/s. The scan parameters for this perfusion were as follows: field of view, 320 mm; matrix size, 512 × 512; tube voltage, 120 kV; and tube current, 150 mA. Finally, dynamic enhanced scanning (80 kV and 100 mAs) was performed.

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The functional CT images were then transferred to a commercial workstation (Syngo, Leonardo Workstation, Siemens) and the data were analyzed using dedicated perfusion software, which generated a quantitative map of the liver perfusion displayed on the monitor by means of a color scale.

2.3. CT image analysis
Two radiologists, with 8 years and 5 years of experience in abdominal CT, reviewed the CT perfusion images and measured the CT perfusion parameters. The region of interest (ROI) was drawn manually in the center of the aorta, portal vein, and spleen. In each patient the slice having the largest diameter of liver tumor was selected to measure CT perfusion parameters. The ROIs were placed within the tumor at least 1 cm away from the tumor border and necrotic tissue, and the vessels were not included in the ROI to the greatest extent possible. ROIs were also placed on liver parenchyma and perfusion parameters were calculated.

Computed tomographic perfusion values of blood flow (BF), blood volume (BV), arterial perfusion (AP), portal perfusion (PP), and hepatic perfusion index (HPI) were calculated in the normal liver parenchyma and HCC samples.

2.4. Statistical analysis
Two radiologists with 8 years and 5 years of experience in abdominal CT evaluated CT perfusion images by consensus. Student's t-test was used to determine the significance between the CT perfusion parameter values of the lesion and the liver parenchyma. The values of CT perfusion parameters were expressed as mean ± SD and P < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS 16.0 (SPSS Inc., Chicago, IL, USA).

3. Results
There were a total of 21 histologically proven HCC lesions; 14 patients had a single lesion, 2 had 2 lesions, and 1 had 3 lesions. The size of the lesions ranged from 2.4 to 7.3 cm (mean: 4.9 cm) in diameter.

On CT perfusion images BF, BV, AP, and HPI values were shown to be significantly higher (P < 0.05) in the HCC lesions than in the surrounding liver parenchyma (Figure). Conversely, PP values were found to be significantly lower (P < 0.05) in HCC relative to liver parenchyma (Table).

4. Discussion
HCC is one of the most vascular solid tumors. It mostly occurs in patients with chronic hepatitis and cirrhosis. The outcome of patients with untreated HCC is very poor (3). One of the important features in staging is tumor vascularity. Conventional cross-sectional imaging methods such as CT and magnetic resonance, as well as imaging with ultrasonography, may not be adequate for detection of tumor-associated vascularity (4). A dysplastic lesion gradually converts to HCC in carcinogenesis. During this process, a gradual increase in neovascularized arteries occurs. CT perfusion imaging is a recently developed noninvasive imaging technique that allows both qualitative and quantitative evaluation of tumor vascularity.

Functional imaging technique with CT allows quantification of tissue hemodynamics by using several perfusion parameters in normal and pathologic tissues. This technique involves multiple serial CT acquisitions acquired with a short interval between each acquisition (5). CT perfusion imaging is performed after the administration of iodinated contrast material. Contrast material is transported to the tissue by blood flow and an exchange between the intravascular space and the extracellular interstitial space occurs. Detailed analysis of liver hemodynamics is obtained by serial images with CT perfusion imaging; hepatic blood flow and portal blood flow are calculated using a color-encoded display of parameters derived from the time–density curve.

Functional evaluation has been done for the cirrhotic liver, liver malignancy, infectious liver disease, and other different diseases (6). Perfusion parameters significantly differed when comparing normal tissue versus tumoral tissue. Blood flow, volume, and permeability values are high because of the development of arteriovenous shunts, dilated capillary beds, and hyperpermeable vessels during neoangiogenesis. CT perfusion was also found to be useful for monitoring anticancer agents against tumor vasculature and having the ability to show changes in tumor vasculature. Response to the treatment is better assessed by alterations in tumor vascularity. CT perfusion imaging has also shown potential in predicting response to antiangiogenic therapies, as demonstrated in HCC, rectal tumors, and other body tumors (7–9).

Sahani et al. reported that CT perfusion imaging is a useful modality to assess tumor vascularity and angiogenesis in advanced HCC (10). Ippolito et al. showed that all the quantitative parameters evaluated [hepatic perfusion, tissue blood volume, HPI, AP, PP, and time to peak (TTP)] were significantly altered in HCC (11). Their study showed that hepatic perfusion, BV, HPI, and AP values were higher, whereas PP and TTP were lower, in HCCs relative to the surrounding liver. In the current study, we could evaluate BF, BV, AP, PP, and HPI in HCC and normal liver parenchyma, and the results were similar to those of the previous study. In our study, we assessed the potential role of CT perfusion imaging in the evaluation of HCC lesions. According to our results, this study showed that the values of perfusion parameters, particularly BF, BV, AP, and HPI, are higher in the lesion compared to the normal liver parenchyma.
Figure. CT perfusion images show the ROIs of normal liver parenchyma (1) and HCC (2). The perfusion parameters of liver (BF, BV, AP, HPI, and PP) are shown in the normal liver parenchyma (1) and HCC (2) (for abbreviations, refer to the text).

Table. Values of perfusion parameters of the patients in normal liver parenchyma and HCC (mean ± standard deviation).

<table>
<thead>
<tr>
<th>Perfusion parameters</th>
<th>Liver parenchyma</th>
<th>Hepatocellular carcinoma</th>
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</thead>
<tbody>
<tr>
<td>BF, mL 100 mL⁻¹ min⁻¹</td>
<td>27.29 ± 13.23</td>
<td>58.17 ± 18.52</td>
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<tr>
<td>BV, mL 100 mL⁻¹</td>
<td>9.07 ± 3.27</td>
<td>16.72 ± 6.31</td>
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<tr>
<td>AP, mL 100 mL⁻¹ min⁻¹</td>
<td>8.17 ± 6.35</td>
<td>59.77 ± 27.12</td>
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<tr>
<td>PP, mL 100 mL⁻¹ min⁻¹</td>
<td>17.53 ± 5.71</td>
<td>0.13 ± 0.09</td>
</tr>
<tr>
<td>HPI, %</td>
<td>27.46 ± 23.87</td>
<td>96.85 ± 12.25</td>
</tr>
</tbody>
</table>

There were some limitations to this study. First, the study had a small group of patients. Second, CT perfusion parameters were not compared with the other markers of angiogenesis, such as microvessel density. Third, the radiation dose for each patient was not assessed, although the estimated effective radiation dose was 6.3–7.2 mSv, on the basis of the parameters used.

This study shows that CT perfusion imaging is a useful tool that may serve as a noninvasive biomarker of angiogenesis. CT perfusion imaging has the ability to evaluate tumor assessment, characterization, and neoangiogenesis, and may even play a role in tumor staging in HCC.

References