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# US-CT 3D dual imaging by mutual display of the same sections for depicting minor changes in hepatocellular carcinoma

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ABSTRACT

The purpose of this study was to evaluate the usefulness of ultrasound-computed tomography (US-CT) 3D dual imaging for the detection of small extranodular growths of hepatocellular carcinoma (HCC). The clinical and pathological profiles of 10 patients with single nodular type HCC with extranodular growth (extranodular growth) who underwent a hepatectomy were evaluated using two-dimensional (2D) ultrasonography (US), three-dimensional (3D) US, 3D computed tomography (CT) and 3D US-CT dual images. Raw 3D data was converted to DICOM (Digital Imaging and Communication in Medicine) data using Echo to CT (Toshiba Medical Systems Corp., Tokyo, Japan), and the 3D DICOM data was directly transferred to the image analysis system (ZioM900, ZIOSOFT Inc., Tokyo, Japan). By inputting the angle number ($x$, $y$, $z$) of the 3D CT volume data into the ZioM900, multiplanar reconstruction (MPR) images of the 3D CT data were displayed in a manner such that they resembled the conventional US images. Eleven extranodular growths were detected pathologically in 10 cases. 2D US was capable of depicting only 2 of the 11 extranodular growths. 3D CT was capable of depicting 4 of the 11 extranodular growths. On the other hand, 3D US was capable of depicting 10 of the 11 extranodular growths, and 3D US-CT dual images, which enable the dual analysis of the CT and US planes, revealed all 11 extranodular growths. In conclusion, US-CT 3D dual imaging may be useful for the detection of small extranodular growths.



## 1. Introduction

Hepatocellular carcinoma (HCC) is one of the most common malignancies worldwide. The majority of patients with small HCCs are not suitable candidates for surgical treatment because of underlying cirrhosis. Several local ablation procedures, such as percutaneous ethanol injection (PEI) [1], microwave coagulation therapy (MCT) [2] and radiofrequency ablation therapy (RFA) [3], have been applied in these patients. The identification of early stage tumors appears to be important to obtain a good outcome after these treatments, as the prognosis of these patients depends on the likelihood of the recurrence of the treated tumor. One of the risk factors for recurrence may be the presence of untreated satellite lesions, which may be too small to be detected using conventional imaging modalities [4–10].

Three-dimensional (3D) sonography is reportedly useful for the visualization of tissue structures and the diagnosis of small lesions [11,12]. However sonography has the disadvantage of not being able to depict a wide area without being influenced by the lungs or intestinal air and bone. Multidetector row CT (MDCT) allows the rapid scanning of large longitudinal volumes and can scan volumes over a large range within a short period of time, providing thin-slice images, and can depict a wide area without being influenced by air and bone. However, only 15% of HCC tumors are detected before liver transplantation [7] using MDCT and CT techniques, which have a sensitivity of only 68% for the detection of malignant tumors in patients with underlying cirrhosis [13].

US-CT 3D dual imaging is a diagnostic imaging support system that can provide the same cross-sectional MPR images on the same screen using DICOM (Digital Imaging and Communication in Medicine) volume data from 3D US and 3D CT [14]. We previously applied this system to provide assistance during HCC treatment using high-intensity focused ultrasound (HIFU) and reported the usefulness of this method [14].

The purpose of the present study was to evaluate the usefulness of US-CT 3D dual imaging for the detection of small extranodular growths of HCC.

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**Table 1**
Baseline clinical characteristics of patients with hepatocellular carcinoma.

| No | Age | Sex | HCV-Ab | HBsAg | Nodule size (mm) | Pathology |
|---|---|---|---|---|---|---|
| 1 | 78 | M | + | – | 63 × 56 | Moderately |
| 2 | 70 | M | + | – | 50 × 48 | Moderately |
| 3 | 42 | M | – | + | 28 × 23 | Moderately |
| 4 | 53 | M | – | + | 35 × 28 | Poorly |
| 5 | 73 | F | + | – | 36 × 32 | Moderately |
| 6 | 53 | M | – | + | 40 × 35 | Moderately |
| 7 | 73 | M | + | – | 35 × 32 | Moderately |
| 8 | 72 | M | + | – | 47 × 27 | Moderately |
| 9 | 66 | F | + | – | 63 × 70 | Moderately |
| 10 | 64 | F | – | + | 30 × 22 | Well |

## 2. Materials and methods

### 2.1. Patients

The study was conducted with the approval of the hospital ethics committee, and each patient signed an informed consent form at the time of enrollment. A total of 18 patients were enrolled in this study. Of the 18 patients, 10 had extranodular growths. The clinical and pathological profiles of the patients with single nodular-type HCC with extranodular growth (extranodular growth) who underwent a hepatectomy between May 2004 and October 2006 were reviewed. An analysis of the patient demographics revealed a male:female ratio of 8:2 and a mean age of 64.4 years (range, 42–78 years). Viral hepatitis was the underlying cause of the liver disease in all the patients (HCV-Ab, 6 patients; HBsAg, 4 patients) (Table 1). Only 1 patient had liver cirrhosis. The maximum diameter of the tumors as measured histologically ranged from 28 to 70 mm (mean, 43.4 mm; SD, 14 mm). The histological features of the tumor were classified into well-, moderately- and poorly-differentiated types in 1, 8 and 1 of the 10 cases, respectively. Eleven extranodular growths were pathologically detected in 10 cases.

### 2.2. Ultrasound imaging

2D US images were acquired at a frequency of 3.5 MHz (Aplio™, Toshiba Medical Systems Corp., Tokyo, Japan). The imaging parameters used for the 3D gray scale US imaging were as follows: a transmission frequency of 3.2 MHz, a mechanical index (MI) of 1.6, an acquisition rate of 19 frames/s, and a gain of 84. 3D volume data were obtained by free hand tilt scanning with a convex type of probe equipped with a 3D sensor (Fig. 1a) while the patients held their breath for 10–12 s [12].

### 2.3. CT imaging

Triple-phase helical CT was performed after overnight fasting using a CT scanner (Light Speed Ultra, GE Medical Systems, Milwaukee, WI, USA) with the patient in a supine position. The contrast medium (Iopamiron; Bracco, Milan, Italy) was injected intravenously. The scanning parameters were as follows: 1.25 mm collimation × 16, a pitch 0.63, 140 kVp, 280 mA, 512 × 512 matrix, and a 1.25 mm reconstruction interval.

### 2.4. US-CT 3D dual imaging

The transmitter (the instrument that produces the magnetic waves) (Fig. 1a) was placed on the left flank of the patient. A 3D magnetic sensor (Fig. 1a) equipped with the previously mentioned US machine was used to obtain the volume data $(x, y, z)$ (Fig. 1b and c). The supine position and breathing protocol were the same as those use for the CT examination. Raw 3D US data was converted to DICOM (Digital Imaging and Communication in Medicine) data using Echo to CT (Toshiba Medical Systems Corp., Tokyo, Japan), and the 3D CT DICOM data was directly transferred to the image analysis system (ZioM900; ZIOSOFT Inc., Tokyo, Japan) [14] (Fig. 2). By inputting the angle number $(x, y, z)$ of the 3D CT volume data into the ZioM900, MPR images of the 3D CT data were displayed in a manner such that they resembled the conventional US images (Fig. 2). To adjust for minute differences in the planes of CT and US images, the intrahepatic portal vein, hepatic vein, gallbladder and diaphragm were used as markers. Less than 30 s was required to process the CT and US images. The 3D images were observed stereoscopically while using opacity control and plane shifting. The resulting images were evaluated independently by each of three authors.

**Table 2**
Detection of extranodular growth using 2D US, 3D US, 3D CT and US-CT 3D dual imaging.

| No | Extranodular growth size (mm) | 2D US[a,c] | 3D US[a] | 3D CT[b] | US-CT 3D dual [b,c] |
|---|---|---|---|---|---|
| 1 | 8 × 8 | – | + | – | + |
| 2 | 11 × 10 | – | + | – | + |
| 3 | 12 × 10 | – | + | – | + |
| 4 | 12 × 10 | – | + | – | + |
| 5 | 15 × 15 | – | + | + | + |
| 6 | 20 × 15 | + | + | + | + |
| | 18 × 15 | + | + | + | + |
| 7 | 10 × 10 | – | + | – | + |
| 8 | 15 × 14 | – | – | + | + |
| 9 | 20 × 18 | – | + | – | + |
| 10 | 10 × 10 | – | + | – | + |

a,b,c: $p < 0.01$.

### 2.5. Histopathology

Resected liver samples were cut on the same plane as viewed using US, and were fixed with 10% formalin. Macroscopic sections were stained with hematoxylin and eosin. Hepatocellular carcinomas of the nodular type were defined as tumors characterized by a clear border between the tumor and the surrounding parenchyma and were subclassified into three forms according to Kanai's classification [15]. The criteria used to identify extranodular growths were assigned according to the classification of the Liver Cancer Group of Japan [16]. The pathologic evaluations were made by two pathologists who were blinded to the imaging findings.

### 2.6. Statistical analysis

Relationships between categorical variables were analyzed using the $\chi^2$ test. A $p$ value of less than 0.05 was considered statistically significant.

## 3. Results

Of the 18 HCC cases, 10 were identified as the extranodular growth type pathological examination. Eleven extranodular growths were pathologically found in 10 cases. Table 2 summarizes the sizes of the extranodular growths and the detectability results for each imaging modality. 2D US was capable of depicting only 2 of the 11 extranodular growths, whereas 3D CT was capable of depicting 4 of the 11 extranodular growths. On the other hand, 3D US was capable of depicting 10 of the 11 extranodular growths, while 3D US-CT dual imaging, which enable the mutual analysis of the same CT and US planes, revealed all 11 extranodular growths. The sensitivity of the 3D US-CT dual imaging was superior to that of 2D US and 3D CT ($p < 0.01$), while the sensitivity of 3D US was also superior to that of 2D US ($p < 0.01$).

The detectability was evaluated according to the size of the extranodular growths, that is, depending on whether the growths