Selective TACE for hepatocellular carcinoma using cone beam CT on a flat detector angiography system: initial experience

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Transcatheter arterial chemoembolization (TACE) is widely performed for unresectable hepatocellular carcinoma [1-6]. Recent meta-analysis of previous randomized controlled trial data of TACE for hepatocellular carcinoma reported that TACE could improve the survival rate [3, 4]. Selective TACE should be performed if possible, in order to avoid toxicity to the surrounding non-cancerous hepatic parenchyma. Matsui et al. [5] and Takayasu et al. [6] reported that subsegmental TACE could improve local control as well as the survival rate.

CT during hepatic arteriography is very useful for detecting hypervascular hepatocellular carcinoma and identifying the feeding vessel [6, 7]. Moreover, a combination of CT hepatic angiography and CT during arteriopentography can improve detection sensitivity and diagnostic accuracy in the case of focal hepatic tumors [7, 8]. However, in many hospitals the patients have to be transferred from the angiography room to a separate CT room for CT hepatic angiography and CT arteriopentography.

Recently, there have been reports on the use of a unified angiography/CT system in which the angiography and CT systems are combined in the same room [6]. However, such systems are only found in a limited number of hospitals, because they are rather expensive and require a great deal of space.

Recent developments in flat panel detector technology and three-dimensional rotational angiography techniques can provide good 3D angiography and cross-sectional, soft tissue imaging on an angiography system. The imaging technique is referred to as cone beam CT [9-11]. Based on the underlying algorithm of cone beam CT proposed by Feldkamp et al. in 1984 [9], cone beam CT on an angiography system was originally performed with an image intensifier [10], but the image quality was not deemed sufficient for clinical use in the abdominal region. In 2006, Hirota et al. first reported initial experience of abdominal interventional radiology procedures using cone beam CT on a flat panel digital angiography system [11].

In this article, we report on the initial experience with selective TACE for hepatocellular carcinoma using cone beam CT with a flat detector angiography system, and describe the utility of the cone beam CT system in this procedure. In accordance with our institutional guidelines, institutional review board approval was acquired for this retrospective report.

Material and methods

Patients

From September 2006 to December 2006, ten patients having suspected hepatocellular carcinoma underwent selective TACE. Immediately before the procedure, cone beam CT was performed during arterial portography and hepatic arteriography.

The patients were six men and four women, ranging in age from 64 to 86 years, with a mean age of 73 years. Child-Pugh classification of all the patients was class A.

The target hepatocellular carcinomas ranged from 5 mm to 37 mm in diameter, with a mean diameter of 16.9 mm. The presence of hepatocellular carcinoma was confirmed using a combination of clinical and radiologic criteria.
For confirmatory imaging studies, these patients also had non-enhanced CT following arterial administration of iodized oil after the TACE procedure.

All patients underwent intravenous contrast-enhanced CT on a 64-channel MDCT scanner within one month prior to TACE. All helical scans were started at the top of the liver and progressed in a cephalocaudal direction. Non-enhanced and two-phase (early phase and portal phase) contrast-enhanced helical scans of the whole liver were obtained. All cases received an injection of 100-140 ml of nonionic contrast agent via a power injector at a rate of 4 ml/s through a 20-gauge plastic intravenous catheter placed in an antecubital vein. Iodized-oil CT was performed using a 4- or 64-channel MDCT scanner within one week after TACE.

**Cone beam CT equipment**

The clinical examination was performed using a single-plane C-arm angiography system with a flat panel detector (Allura Xper FD20, Philips Medical Systems, Best, the Netherlands). The flat panel detector in this system uses an indirect method with X-ray conversion via cesium iodide (CsI). The detector has a 38 × 30 cm² field of view and a 2480 × 1920 pixel matrix with a 154 μm pixel pitch.

The C-arm system has two different movement modes for acquisition in three-dimensional rotational angiography: a “propeller” movement at a speed of 55°/s passing through 240 degrees of arc, and a “roll” movement at a speed of 30°/s through 180 degrees of arc.

The system is equipped with software for 3D rotational angiography and cone beam CT soft tissue imaging (XperCT, Philips Medical Systems).

The cone beam CT acquisition data is acquired in the propeller mode using the following parameters:
- Source-detector distance: 1200 mm
- Source-rotation axis distance: 810 mm
- Detector-rotation axis distance: 390 mm
- X-ray tube voltage: 117 to 123 kVp
- X-ray tube current: 50 to 320 mA
- Rotation speed: 20°/sec
- Rotation duration: 10 sec.

The total arc trajectory range of 240° remains unchanged, but the images are acquired over 200°. The rotational image frames are acquired in 1024 × 1024 matrix format with a pixel depth of 14 bits. A total number of 310 frames are used to generate the CT data.

The acquisition frames are transferred via an optical link in real time to the 3DRA workstation (Philips 3DRA workstation, Rel 6.2; Dell Precision 670 workstation, Round Rock, TX/USA) where the reconstruction starts as soon as the first image is received. The total reconstruction time (including transfer time) depends on the number of frames used for the CT reconstruction generation, and in this case is 90 sec.

The reconstructed CT data set has a 256 × 256 × 198 pixel matrix and is displayed as a cylindrical volume with a diameter of 250.5 mm and a height of 193.5 mm. High-resolution 3D maximum intensity projection (MIP) hepatic arteriography images can also be reconstructed and displayed, with 512 × 512 pixel matrices. Image browsing can be performed using the multi-planar reformatting (MPR) and MIP techniques.

**Cone beam CT technique during angiography and TACE**

A 4 Fr catheter or a combination of a 4 Fr catheter and a 2.1-2.2 Fr microcatheter were used. The catheter tip was positioned in the target artery using the Seldinger technique via the right or left femoral artery. Both cone beam CT arterial portography and cone beam CT hepatic angiography were performed immediately before TACE.

For cone beam CT arterial portography, the catheter tip was positioned in the superior mesenteric artery. Cone beam CT arterial portography was performed 30 seconds after injection of 40 ml of contrast agent (Iomeron 300: Iomeprol 300 mg I/L, Eisai, Tokyo, Japan) at an injection rate of 2 ml/s via the superior mesenteric artery.

For cone beam CT hepatic angiography, the catheter tip was placed in the proper hepatic artery or replaced right hepatic artery. Cone beam CT hepatic angiography was performed immediately after injection of 15 ml or 23 ml of contrast agent at an injection rate of 1 or 1.5 ml/s via the common hepatic artery, the proper hepatic artery, or replaced hepatic artery.

The first and second phase of cone beam CT hepatic angiography was performed at 5 and 40 sec after the start of contrast agent injection.

After the assessment of the number and size of the lesions and the feeding artery by cone beam CT arterial portography and hepatic angiography, a microcatheter was inserted in the feeding artery to the target hepatocellular carcinoma lesions, and an emulsion of 1-4 ml iodized oil (Lipiodol:...
Andre Guerbet, Aulnay-sous-Bois, France) and 10-40 ml epirubicin hydrochloride (Farmorubicin: Kyowa Hakko, Tokyo, Japan) was administered through a subsegmental or segmental hepatic artery. Embolization of the feeding hepatic artery was then performed with gelatine particle embolization material (Gelpart®: Nippon Kayaku Co. Ltd., Tokyo, Japan).

Cone beam CT was performed immediately after TACE without contrast agent injection, in order to confirm accumulation of iodized oil in the hepatocellular carcinoma nodules.

**Assessment**

The numbers of hepatocellular carcinoma nodules that were detected by cone beam CT during angiography (cone beam CT arterial portography and double-phase cone beam CT hepatic angiography) and by intravenous contrast-enhanced CT were counted and compared with each other.

Secondly, the information provided by cone beam CT hepatic angiography and two-dimensional digital subtraction angiography (2D-DSA) was compared as described below.

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**Figure 1.** A 71 year old woman with two hepatocellular carcinomas in the posterior segment.

**Figure 1a.** Cone beam CT during arterial portography (cone beam CT arterial portography) shows portal perfusion defect in segment 7.

**Figure 1b.** The first-phase image of cone beam CT during hepatic arteriography (cone beam CT hepatic angiography) shows tumor enhancement in segment 7.

**Figure 1c.** On the second-phase image of cone beam CT hepatic angiography, the tumor shows ring enhancement.

**Figure 1d.** Cone beam CT after TACE procedure shows good accumulation of the iodized oil in the tumor.

**Figure 1e.** Cone beam CT arterial portography shows small portal perfusion defect (arrow) in segment 6.

**Figure 1f.** The first-phase image of cone beam CT hepatic angiography shows tumor enhancement (arrow) in segment 6.

**Figure 1g.** In the second-phase image of cone beam CT hepatic angiography, the tumor shows ring enhancement (arrow).

**Figure 1h.** The early-phase image of intravenous contrast-enhanced conventional CT does not show the tumor in segment 6.
We defined a grading score of 1 (no visualization of tumor stain and no identification of the feeding artery), 2 (visualization of tumor stain, but no identification of the feeding artery), and 3 (visualization of tumor stain and identification of the feeding artery). Finally, we evaluated whether the image quality of iodized-oil cone beam CT was equivalent to that of iodized-oil CT within one week after TACE with respect to spatial resolution.

Results

The number of hepatocellular carcinoma nodules detected by the combination of cone beam CT arterial portography and cone beam CT hepatic angiography was 16, while the number detected by intravenous contrast-enhanced CT was 13. In three patients, small hepatocellular carcinomas, less than 10 mm in diameter, could be detected by the combination of cone beam CT arterial portography and cone beam CT hepatic angiography (Figure 1).

In the second-phase images of cone beam CT hepatic angiography, all hepatocellular carcinoma nodules showed rim enhancement, and the perfusion abnormality in one patient showed prolonged enhancement (Figure 2).

In this patient, the second-phase images of cone beam CT hepatic angiography could differentiate hepatocellular carcinoma nodule from the perfusion abnormality area.

In a comparison of 2D DSA and high-resolution 3D-MIP hepatic arteriography (Figure 3) in our group of ten patients with known lesions, the image quality score with respect to tumor stain and feeding artery depicted by each image type was as shown in Table 1.

One week after TACE, the image quality of iodized-oil cone beam CT showing accumulation of iodized oil in the target lesions was equivalent to that of iodized-oil CT in all ten patients (Figure 1d).

Discussion

In selective TACE for hepatocellular carcinoma, precise assessment of the number, size, location and the feeding artery of the target lesions is important [6-8]. It is therefore desirable to perform CT arterial portography and CT hepatic angiography before TACE. However, performing CT scans in addition to a DSA procedure requires more contrast agent, more radiation exposure and more time.

With cone beam CT arterial portography and cone beam CT hepatic angiography on the angiography system itself, it is not necessary to move the patients to the CT room during the TACE. Even though cone beam CT quality is inferior to CT in some respects, cone beam CT provides important information without the need to perform a CT scan [11].

In our system, the total time needed from the start of the rotational angiography to the reconstruction on the workstation is 90 sec. This extra time did not noticeably hold up the procedure. Thus, cone beam CT arterial portography and cone beam CT hepatic angiography may actually save time in the TACE procedure, as well as reducing the quantity of contrast agent and the amount of radiation exposure required.

In our experience with the cone beam CT system, the number of hepatocellular carcinoma nodules detected with a combination of cone beam CT arterial portography and cone beam CT hepatic angiography prior to TACE was greater than that obtained with intravenous

<table>
<thead>
<tr>
<th>Image type</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
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<tr>
<td>2D DSA</td>
<td>4 patients</td>
<td>4 patients</td>
<td>2 patients</td>
</tr>
<tr>
<td>3D MIP</td>
<td>0 patients</td>
<td>1 patient</td>
<td>9 patients</td>
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Table 1. Comparison of image quality scores of 2D DSA and 3D MIP in a group of ten patients with known lesions: Grade 1: No visualization of stain or feeding artery. Grade 2: Visualization of tumor stain only. Grade 3: Visualization of tumor stain and feeding artery.
contrast-enhanced CT. In three out of ten patients, small hepatocellular carcinoma nodules, which were small intrahepatic metastases, could be detected by a combination of cone beam CT arterial portography and cone beam CT hepatic angiography.

We anticipate that a combination of cone beam CT arterial portography and cone beam CT hepatic angiography on the angiography system may improve detection of hepatocellular carcinoma nodules without the need for conventional CT arterial portography and CT hepatic angiography. However, cone beam CT hepatic angiography, consisting of the hepatic arterial dominant phase images only, may show many false positive lesions, due to perfusion abnormalities that are not caused by a tumor, as described by Murakami et al. when reporting on the CT hepatic angiography examination for detection of hepatocellular carcinoma [8]. They reported that double phase CT hepatic angiography, in which the phase with washout of contrast agent from the tumor was added to the hepatic arterial dominant phase, could improve the diagnostic accuracy of hepatocellular carcinoma. We therefore performed a second-phase cone beam CT hepatic angiography in addition to the first-phase cone beam CT hepatic angiography at 40 sec after the start of the contrast agent injection. This corresponded to 25 sec after the finish of the contrast agent injection, in line with Ueda et al., who reported that the corona enhancement of hepatocellular carcinoma appeared about 23 sec after the start of the contrast agent injection [12].

In one patient, we could differentiate perfusion abnormality from the hepatocellular carcinoma nodules in the second-phase cone beam CT hepatic angiography. We think that performing both double-phase cone beam CT hepatic angiography and cone beam CT arterial portography at the time of TACE provides the interventional radiologists with more accurate information on the focal liver lesions and the precise segment, enabling them to perform selective TACE.

It is sometime difficult to identify the artery that feeds the target lesions in TACE using the conventional DSA system. Three-dimensional rotational angiography (3D-RA) has been recently introduced for application in the cerebral and abdominal regions, but Tanigawa et al. reported decreased imaging quality for the tumor blush and feeding vessels in the 3D-RA images when compared with conventional anteroposterior DSA views [13].

In our experience, the cross-sectional images of cone beam CT hepatic angiography and reconstructed high-resolution 3D-MIP hepatic arteriography with a 512 × 512 pixel matrix demonstrated good visualization of the tumor blush and feeding vessels in nine out of 10 cases.

It takes several extra minutes to generate high-resolution 3D-MIP hepatic arteriography in our cone beam CT system. However, the time needed to render the high-resolution 3D-MIP hepatic arteriography seems acceptable for clinical use and has several benefits. The advantage is that 3D MIP eliminates the need for multiple DSA and fluoroscopic views, and as a result decreases the radiation exposure for patients and physicians.

We usually use iodized-oil CT to evaluate the technical success of TACE for hypervascular hepatocellular carcinoma. Because most hepatocellular carcinoma lesions are fed by the hepatic artery and are hypervascular, intraarterially administered iodized oil is preferentially deposited in the lesions. In our experience, the cone beam CT system can confirm the accumulation of the iodized oil in all cases by iodized-oil cone beam CT. Therefore, iodized-oil cone beam CT can be the alternative to conventional iodized-oil CT.

In conclusion, cone beam CT arterial portography and cone beam CT hepatic angiography with a flat panel detector angiography system are of sufficient quality to detect the hepatocellular carcinoma nodules and the feeding vessels for selective TACE, without performing a CT scan in addition to the DSA procedure.

Cone beam CT with a flat panel detector angiography system has the potential to become a useful modality in selective TACE for hepatocellular carcinoma.
References


