Interventional oncology on a C-arm system with XperCT: targeting liver cancer

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Imaging plays a key role in interventional oncologic procedures such as transcatheter arterial chemoembolization (TACE) and percutaneous portal vein embolization (PVE). TACE delivers highly concentrated doses of chemotherapy to the tumor bed, while sparing the surrounding hepatic parenchyma [1, 2]. TACE has gained wide acceptance over the past twenty years and is now considered the main therapy for unresectable primary and metastatic liver cancer.

PVE leads to atrophy of the embolized lobe and compensatory hypertrophy of the remnant liver, which may prevent liver failure after hepatic resection, and is thus performed as a preoperative treatment of resectable liver tumors [3-5].

The two procedures, like other interventional procedures, can be divided into the following four stages:
• Planning
• Targeting/guidance
• Treatment/monitoring
• Evaluation/confirmation.

Planning
In the planning stage, the arteries or veins and the tumors are mapped, and the catheter position for treatment is determined based on this information.

Treatment/guidance
In the targeting/guidance stage, contrast solution is injected from the catheter at the proposed treatment site, clearly identifying the tumor, thereby allowing precise mapping of the tumor and visualization of the area to be treated.

Treatment/monitoring
In the treatment/monitoring stage, the treatment progress is monitored. For example, the iodized chemotherapy mixture is injected and monitored under fluoroscopic control as it moves down the arteries, and lodges in the tumor.

Evaluation/confirmation
In the evaluation/confirmation stage, the final deposition of the treatment mixture is confirmed.

Recent advances in three-dimensional (3D) imaging with C-arm systems can potentially improve interventional radiology procedures. Using rotational angiography with a flat-panel detector, a volume-rendered 3D image of the patient can be obtained, which has been shown to aid the interventional radiologist during a TACE procedure in cases of complex vascular anatomy [6]. Until recently, however, these systems had insufficient low-contrast resolution and could only visualize high-contrast objects such as arteries. Tumor blushes were usually not visible.

More recently, 3D soft tissue imaging with C-arm angiographic computed tomography (CCT) system has been developed. In this report, we outline the advantages and the challenges we found utilizing CCT for PACE and PVE procedures in four patients. The Institutional Review Board of our institution approved this study.

Soft tissue imaging C-arm CT (CCT) technique

An angiographic system (Allura Xper FD 20; Philips Medical Systems, Best, the Netherlands) was used. This system is equipped with a flat-panel detector and a ceiling mounted motorized C-arm with the rotational angiography (RA) option and the capability of reconstructing the soft tissue images.

For each CCT acquisition, the area of interest was positioned near the system isocenter and scanned with the "propeller" movement (i.e. around the patient's longitudinal axis) through 240º. The scan time was 10 or 20 seconds, depending on the number of acquired images. A series of up to 310 or 620 images were collected at a frame rate of 30 frames per second. Each frame had a matrix size of 1024 × 1024 with a depth of 14 bits. The system transferred the projection image data to a workstation in parallel to the acquisition for volume data reconstruction using commercially available software (XperCT Release 1; Philips Medical Systems; Best, the Netherlands).

▶ **Imaging plays a key role in interventional oncological procedures such as TACE and PVE.**

▶ **The procedures were performed using an Allura Xper FD20 C-arm angiography system.**

The volume data set was reconstructed by weighted Feldkamp algorithm [7-9] displayed about 90 seconds after the end of rotational scan. Each 3D image covered a volume of 25 × 25 × 19 cm with a matrix size of 256 × 256 × 198. The images were typically viewed as transaxial slices at our institution, as these provide the best comparison with CT and MR images; other view angles are used to obtain the best view of the tumor and iodine distributions.

Case studies
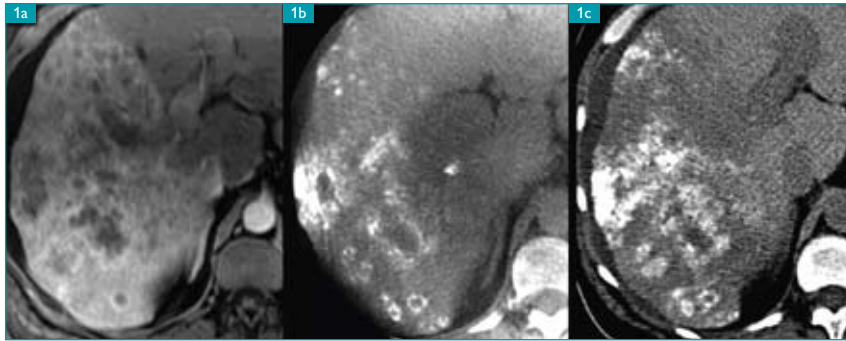
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Figure 1. Case 1: a 49 year old man with multifocal hepatocellular carcinoma (HCC).

Figure 1a. Pre-TACE MR.
Figure 1b. Post-treatment CCT.
Figure 1c. Post-TACE CT.

Case 1

The first patient was a 49 year old man with multifocal hepatocellular carcinoma (HCC), who had already undergone one previous chemoembolization procedure. MR imaging of the liver revealed a large mass with multiple satellite lesions occupying almost the entire right lobe, demonstrating residual enhancement of the dominant lesion ranging between 25 and 50% on the arterial phase of the gadolinium-enhanced T1 sequence (Figure 1a) indicating a follow-up TACE procedure.

Through a 5-F vascular sheath that was placed into the right common femoral artery, a 5-F glide Simmons-1 catheter (Terumo, Somerset, NJ, USA) was advanced to select the celiac axis. Digital subtraction angiography (DSA) of the SMA showed classic hepatic vascular anatomy. The catheter was then navigated into the right hepatic artery over a 0.035 inch guide wire advanced coaxially through the Simmons catheter. The DSA images taken during the targeting phase showed tumor blush, confirming the treatment location.

The patient was treated with 9 cc of a standard chemotherapeutic preparation comprising 100 mg Cisplatin, 50 mg of Doxorubicin (Adriamycin; Pharmacia-Upjohn, Kalamazoo, MI, USA), and 10 mg of Mitomycin-C (Bedford Laboratories, Bedford, OH, USA) mixed with an equal volume of Lipiodol (chemotherapy: Lipiodol), making a total of 18 cc. The mixture was injected slowly by hand in order to avoid reflux.

The injection was followed by infusion of 4 cc of embosphere particles, 100-300 microns in size, and 18 cc of 1% lidocaine to slow down arterial inflow, prevent washout of the chemotherapeutic mixture, and ease the patient's discomfort.

An anterior-posterior single shot image was taken to evaluate the chemotherapy/lipiodol mixture deposition. This two-dimensional image did not have enough contrast resolution to show the tumor stain. However, the subsequent 3D CCT images revealed adequate lipiodol deposition in a wide region of the right hepatic lobe (Figure 1b). A comparison of the evaluation image with an arterial phase contrast-enhanced MR image showed a striking correlation between the pattern of lipiodol deposition (Figure 1b) and the pattern of arterial tumor enhancement in the liver as revealed in the MRI (Figure 1a).

The CCT images confirmed during the procedure that, despite the non-selective nature of the treatment, the chemotherapeutic mixture was preferentially taken up by the tumor, suggesting a successful treatment. A standard non-contrast-enhanced CT performed one day after treatment (Figure 1c) verified the pattern of Lipiodol deposition which the post-treatment CCT images demonstrated. The post-TACE CT images showed an almost identical pattern of Lipiodol deposition in the right lobe of the liver (Figure 1c). There is strong agreement in the location, extent, intensity, and pattern of uptake within each lesion. This indicates that the post-treatment CCT scan may allow an adequate evaluation of TACE procedures while the patient is still on the catheterization table.

Case 2

A 49 year old woman with liver metastasis of adenocarcinoma of an unknown primary origin agreed to receive repetitive TACE sessions as a palliative option. MR imaging of the liver was performed three days before the chemo-embolization procedure; it showed a lesion occupying the entire left lobe with a T1-hypointense and a heterogeneous T2 signal. Multiple hypointense lesions presented in the right lobe (Figure 2a).

Through a 5-F vascular sheath that was placed into the right common femoral artery, a 5-F glide Simmons-1 catheter was advanced to select the superior mesenteric artery and the celiac axis. The DSA showed a classic hepatic vascular anatomy with a patent portal vein. After direct visualization of the celiac axis, a 3-F microcatheter (Hi-Flo Renegade; Boston Scientific, Natick, MA) was coaxially advanced

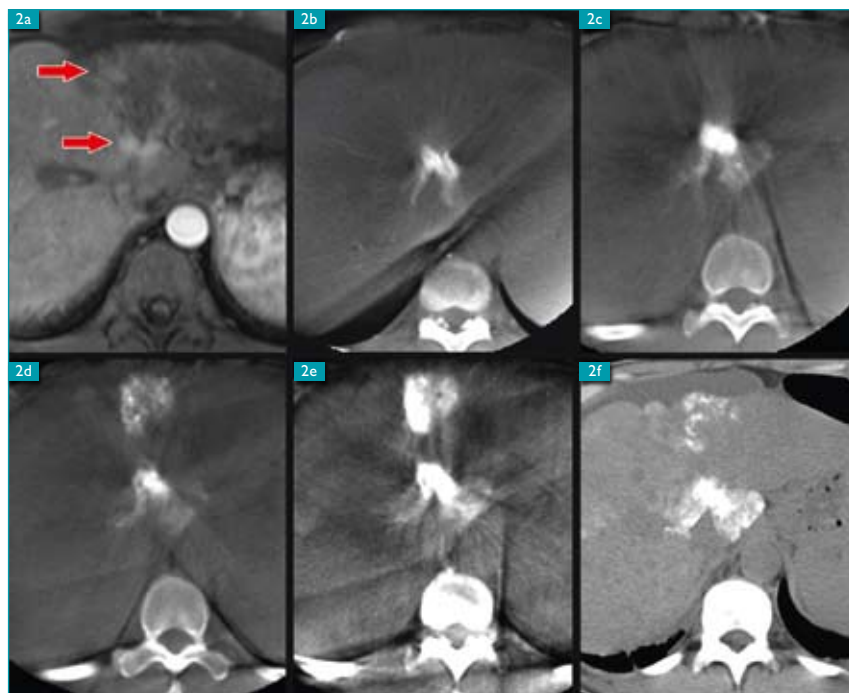through the Simmons catheter over a 0.018-inch guide wire into the left hepatic artery.

To verify the treatment location, a contrast-enhanced CCT scan was performed. 8 cc of contrast medium (Hypaque, Amersham Health, Princeton, NJ, USA) were injected at a rate of 2 cc/s. The scan did not begin until five seconds after the end of the contrast injection, to allow contrast to clear from the major arteries. The reconstructed image showed a partial tumor blush near the portal vein, without any peripheral tumor opacification (Figure 2b) as would be expected from the pre-TACE MRI scan (Figure 2a).

The decision was made to slowly inject the half of the entire therapeutic mixture from this location under fluoroscopy, avoiding reflux: 3.5 cc of chemotherapy with 50 mg Cisplatin, 25 mg of Doxorubicin, and 5 mg of Mitomycin-C mixed with a ratio of 4:1 (chemotherapy: Lipiodol), making a total of 4.5 cc. This was followed by 2 cc of embospheres measuring 100-300 microns in size, and 10 cc of 1% lidocaine. This first half of the treatment was evaluated with a CCT scan without additional injection of contrast. This scan showed an excellent concentration of the chemoembolization mixture at the first target location, indicating the success of the first half of the treatment (Figure 2c).

The artery that supplied the peripheral portion of the lesion was identified on DSA views and a microcatheter was advanced into that artery. Subsequent DSA views showed the peripheral tumor blush, verifying the selection of the appropriate feeding artery. A CCT scan was performed with the same contrast protocol as the DSA run, with a scan delay of 4 seconds after the end of the contrast injection (Figure 2d).

A subsequent second post-treatment CCT scan showed Lipiodol deposition in the left anterior portion of the targeted lesion without enhancement of the stomach wall (Figure 2e). The quality of this image is lower than in other CCT images, due to the patient's breathing. This is a risk in all abdominal CCT scans. Nonetheless, despite the presence of the respiratory motion artifact, a reasonable correlation was observed between the final CCT and contrast enhanced MR images (Figure 2a) with respect to the location, size and shape of tumors, which indicated the success of the procedure.

A standard non-contrast CT image performed the day after the procedure (Figure 2f) showed

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Figure 2. Case 2: a 49 year old woman with liver metastasis of adenocarcinoma.

Figure 2a. Pre-TACE MR image.
Figure 2b. Targeting CCT image.
Figure 2c. Mid-treatment CCT image.
Figure 2d. Targeting CCT image.
Figure 2e. Post-treatment CCT image.
Figure 2f. Post-TACE CT image.

a lipiodol deposit pattern very similar to that in the post-treatment CCT images.

In this case, contrast-enhanced CCT scans predicted the result of the TACE procedure before starting the treatment. A mid-treatment CCT scan verified the on-going treatment in the middle of procedures and allowed us to adjust the treatment. Finally, a post-treatment exam confirmed the treatment.

Case 3
This is a 43 year old woman with a metastatic renal tumor in the liver who previously had two TACE treatments. After the previous TACE treatments, the patient suffered from nausea, vomiting, and loss of appetite for three days post-treatment. MR imaging of the patient taken seven days before the third TACE found the dominant mass in the left lobe (Figure 3a, arrows).

Initial treatment in Case 3 was similar to those in case 2. Once the micro-catheter was in place, a selective arteriogram DSA showed backflow to an artery, which did not appear to feed the tumor, just proximal to the catheter tip. Given the patient's history of gastric complications and sensitivity, and the risk that this artery might be an accessory left gastric, a targeting CCT scan was performed with 15 cc of contrast injected over 5 seconds. The scan began 5 seconds after the end of the injection and continued over the next 10 seconds.

The targeting CCT images (Figure 3b) showed that the catheter was well placed: the entire tumor can be seen clearly outlined by contrast

indicating that there are no accessory feeding arteries. However, there was significant enhancement of the stomach due to backflow from the catheter through the (now confirmed) accessory left gastric (arrows).

Having confirmed the risk of backflow through the accessory left gastric, extra care was taken during the injection of chemotherapy: 9 ml containing 100 mg of Cisplatin, 50 mg of Adriamycin, 10 mg of Mitomycin-C and 5 ml of Lipiodol followed by 20 ml of 1% lidocaine and 2 ml of 300-500 micron embospheres.

A final single-shot image taken after treatment showed strong uptake in the tumor, but could not confirm uptake to the stomach, nor could it confirm that the entire tumor had been successfully targeted. In contrast, subsequent evaluation post-TACE CCT images showed no enhancement of the stomach (Figure 2c) confirming that treatment had avoided backflow through the accessory left gastric artery. A comparison of the evaluation scan with the MRI (Figure 2a) also showed that the entire tumor had been treated during. The complete coverage of the tumor and lack of deposition to the stomach were confirmed by CT the next day (Figure 2d).
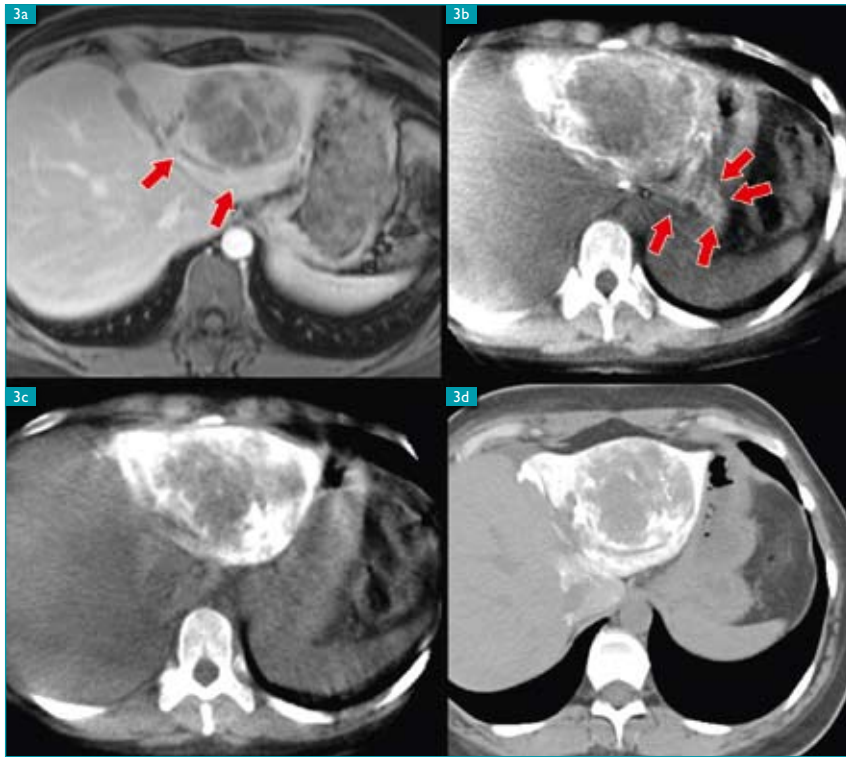
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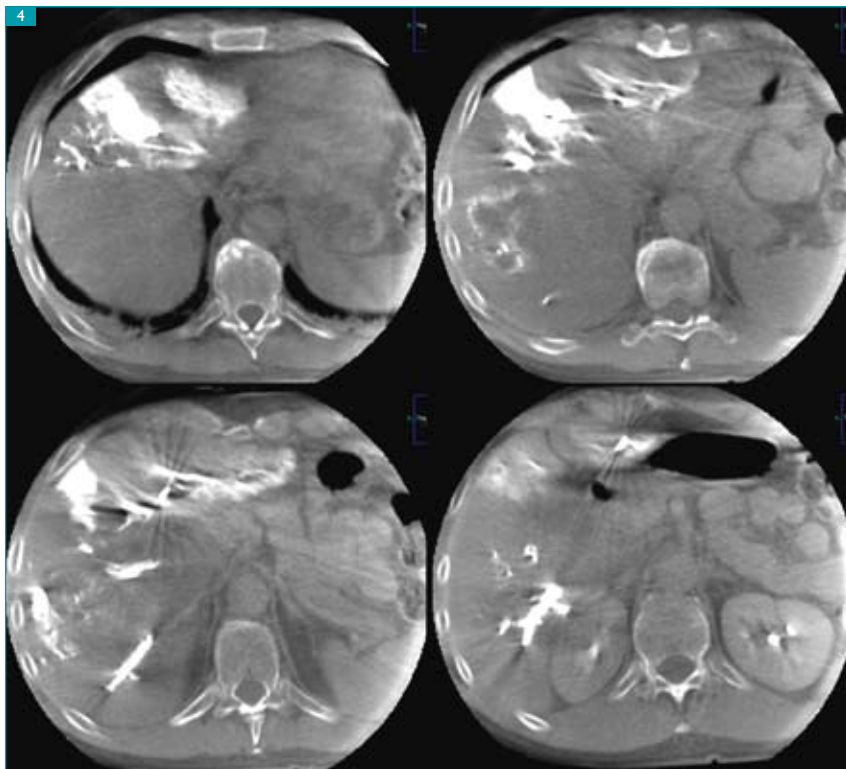Figure 3. Case 3: a 43 year old woman with a metastatic renal tumor in the liver.

Figure 3a. Pre-TACE MR image.
Figure 3b. Targeting CCT image.
Figure 3c. Post-treatment CCT image.
Figure 3d. Post-TACE CT image.

Figure 4. Case 4: a 59 year old man with an HCC in the right hepatic lobe. Contrast-enhanced CCT images.
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Case 4
A 59 year old man with an HCC in the right hepatic lobe underwent a PVE for potential liver resection. Under ultrasound guidance, the peripheral anterior right portal vein was transhepatically accessed with a 21-gage trocar needle of the Jeffrey's set. The Jeffrey's set was then introduced over a 0.018-inch guide wire; then a 0.035-inch guidewire (Terumo, Tokyo, Japan) was introduced through the Jeffrey's set. The guide wire was advanced into the main portal vein through an angled-tapered Glide catheter. After the Glide catheter was exchanged for a 5 Fr. Pigtail catheter, a portogram was performed.

Under ultrasound guidance, the central left portal vein was transhepatically accessed with a 21-gage trocar needle. The Jeffrey's set was then introduced over the 0.018-inch guide wire. Using a combination of 5 Fr Glide catheter and 0.035 inch Glide wire, access into segments 5, 6, 7, and 8 was accomplished. A portogram CCT image was obtained to confirm the catheter location.

Through the Glide catheter, a ratio of 4:1 N-Butyl Cyanoacrylate to lipiodol was injected into the segments 5 through 8 with sterile H_2O as flush. A final portogram CCT image demonstrated preservation of segments 4a, 4b, 2 and 3 with positive enhancement and embolized segments 5, 6, 7, and 8 with negative enhancement (Figure 4).

The volume of the left lobe of the liver was measured three times on MR images: a baseline, one month before the PVE procedure, and one month after the procedure. The results were:

- Baseline 403 cc (segment I, 16 cc; segments II and III, 161 cc; segment IV, 226 cc)
- PVE -1 month 475 cc (segment I, 22 cc; segments II and III, 227 cc; segment IV, 226 cc)
- PVE +1 month 689 cc (segment I, 29 cc; segments II and III, 334 cc; segment IV, 326 cc.

A significant 45% increase of the left lobe volume was achieved.

Discussion

The integration of recently developed volumetric scanning capabilities into interventional radiology procedures has several potential benefits. The soft tissue CCT imaging allows detailed tumor targeting, accurate treatment planning, monitoring of the treatment, as well as immediate post-procedure imaging confirming technical success of the treatment. Lipiodol distribution pattern of post-treatment CCT scans for all three patients, showed excellent correlation with gadolinium distribution of pre-TACE MR images and the Lipiodol deposition of post-TACE CT images obtained one day after the procedure. In cases 2 and 3, CCT scans were used in the targeting, mid-treatment, and evaluation phases.

The targeting CCT scan used contrast medium to predict where the Lipiodol would go during treatment, resulting in a more complete targeting and treatment. In both cases, the post-treatment evaluation scan demonstrated an excellent correlation with the post-treatment non-enhanced liver CT scan that was performed the next day. This demonstrates that the CCT scan may replace this scan as a qualitative means of assessing treatment success. Contrast enhanced CCT scans in case 4 performed after the embolization procedure, demonstrated that both positive and negative enhancement can be used to confirm the extent of portal vein embolization. Abdominal CCT still does not have the image quality equivalent to the standard diagnostic CT; it still suffers from artifacts due to breathing, truncation, scattered radiation, beam hardening, heart motion, and blood pulsation. We are currently investigating the optimal strategy to minimize these artifacts, such as for example giving clear instructions to the patient, and imaging at maximum inspiration. Such tactics can help reduce breathing artifacts, while proper patient positioning can reduce truncation artifacts. The appropriate contrast protocol can enhance desired features while reducing artifacts from distant dense regions.

CCT scans may become an important tool for the interventional oncologist. Acquiring CT-like images during the procedure provides a unique capability to predict expected therapeutic effects beforehand at the planning and targeting phases. Moreover, it also allows us to compare the intermediate results of treatment during the procedure by mid-treatment scan, which gives us a chance to adjust the treatment accordingly. The instant feedback after a procedure at the evaluation phase can also provide an important reassurance to the physician and patient.

▶ **Acquiring CT-like images during the procedure provides a unique capability to predict therapeutic effects.**

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