

# Selective doxorubicin drug eluting beads chemoembolization of hypovascular hepatocellular carcinoma using cone beam computed tomography

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## Abstract

Hepatocellular carcinoma (HCC) of the liver is the third most common cause of cancer-related deaths in the world. Only one-third of patients with HCC are suitable candidates for hepatic resection. Transarterial chemoembolization (TACE) is performed in unresectable HCC. Drug-eluting beads (DEB) TACE is a modification of TACE, in which doxorubicin beads are used as embolizing material. These beads deliver the drug and embolize the vessels; however, it carries the risk of non-target embolization and it is difficult in cases with absent arterial blush on digital subtraction angiography (DSA). This is resolved using C-arm cone-beam computed tomography in the DSA suite. It identifies the tumor-feeding vessels, their area of supply, and differentiates between tumor and normal liver parenchyma. In addition, it is very useful in the embolization of hypovascular HCC. It helps and guides the radiologist in performing TACE effectively and also prevents non-target embolization of normal liver parenchyma.

**Key words:** Cone-beam computed tomography; hepatocellular carcinoma; transarterial chemoembolization

## Introduction

Worldwide, there are approximately 500,000 cases of hepatocellular carcinoma (HCC) per year, making it the fifth most common cancer in the world.<sup>[1]</sup> Typical HCCs are hypervascular during the arterial phase and show washout in the portal venous phase. Hypovascular HCCs enhance minimally because of poor arterial blood supply. Transarterial chemoembolization (TACE) is a treatment option for unresectable HCC.<sup>[2]</sup> Drug-eluting beads (DEB) TACE is a modification of conventional TACE, in which doxorubicin DEBs act as the embolizing material.<sup>[3]</sup> As

DEBs are expensive and permanently embolize the vessel, there is a need to deliver the beads into the tumor vessels superselectively to prevent the risk of missing the tumor or causing incomplete embolization of the tumor. This can be made feasible by using contrast-enhanced cone-beam computed tomography (CT), which also helps prevent embolization of normal liver parenchyma. In this case report, we demonstrate the utility of cone-beam CT for selective chemoembolization of the tumoral vessels.<sup>[4]</sup>

## Case Report

A 60-year-old male with child-pugh class A cirrhosis was detected to have elevated  $\alpha$ -fetoprotein levels (180 international units/ml) during routine screening. He was a chronic alcoholic with a history of coronary artery disease. He underwent biphasic contrast-enhanced computed tomography and magnetic resonance imaging, which showed a 6 cm  $\times$  5.6 cm hypodense exophytic lesion in segments five and eight of the liver, with minimal enhancement in the arterial phase [Figure 1A]. There was

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no significant washout or enhancement in the portal venous phase [Figure 1B]. Mild hypertrophy of the left lobe was also observed, with a few collaterals at the porta and splenic hilum. Fine-needle aspiration of the lesion confirmed the lesion to be HCC.

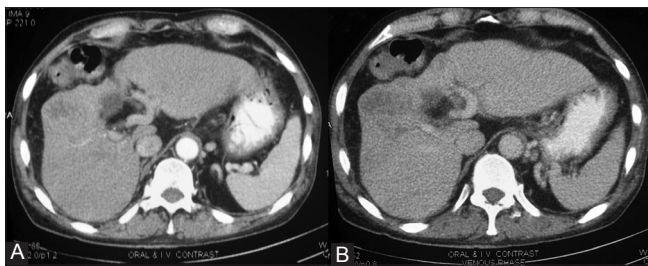
As the patient was unfit for surgery, we decided on DEB TACE. He was taken up for DEB TACE in the digital subtraction angiography (DSA) suite. Selective angiograms of the celiac artery and hepatic artery [Figure 2] were performed, which showed no significant abnormal blush from the branches of the right hepatic artery (RHA). We decided to selectively cannulate the RHA branches. We first cannulated the medial-most branch, which showed mild abnormal blush, although it was not in the anatomical region of the tumor [Figure 3A]. Before embolization we carried out XperCT™ (Philips Healthcare, Best, The Netherlands) acquisition, which showed that the vessel was exclusively supplying the normal hepatic parenchyma [Figure 3B]. The possibility of embolizing this normal vessel was thus avoided. XperCT™, a kind of cone-beam CT, was performed with a flat-panel detector C-arm angiography system. Scanning was performed with propeller movement, with an acquisition time of 10 s, a detector size of 30 cm × 38 cm, a fixed tube-detector distance of 0.9 m, a total scanning angle of 240°, and 2480 × 1920 pixel matrix with a 154 µm pixel pitch. Fifteen milliliters of contrast was injected at an injection rate of 1 ml/s in the selectively cannulated hepatic artery branch. The XperCT™ scans were acquired approximately 6 s after the start of injection. The raw datasets from the angiographic

C-arm system were sent to a dedicated workstation and reconstructions were performed to generate the volume data. The multiplanar reconstruction (MPR) and maximum intensity projection (MIP) images were studied and the vessels to be embolized were selected based on these images.

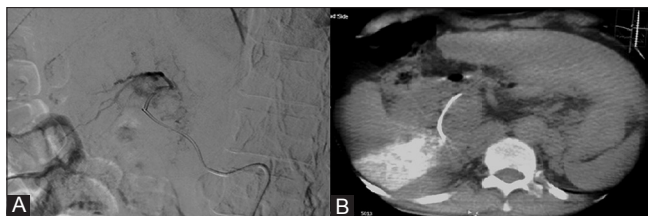
Next, we selectively cannulated the middle and the lateral branches of the RHA and these were seen to be supplying the tumor. Vascular supply to the tumor by these vessels was confirmed on XperCT™ [Figure 4A and B] and we selectively embolized these vessels using DEB. Using XperCT™ we could deliver the drug precisely and accurately into the tumor-feeding vessels and prevent unnecessary embolization of normal hepatic parenchyma. No procedure-related complications occurred. Post-procedure follow-up CT showed almost complete tumoral necrosis [Figure 5].

## Discussion

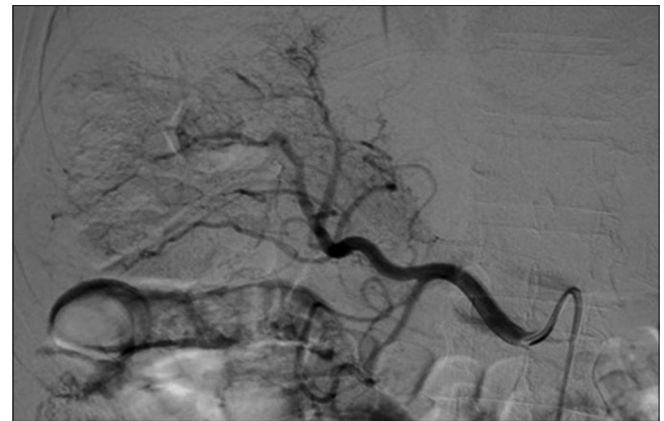
HCC is now the leading cause of death in patients with cirrhosis, and its incidence is on the rise. Treatment options include resection or transplant; however, in patients who are unfit for surgery, alternative procedures for treatment can be used; these include chemoembolization, radiofrequency ablation, and alcohol ablation. Conventional TACE is catheter based and involves the injection of chemotherapeutic agents, with or without lipiodol and embolic agents, into the branch of the hepatic artery that feeds the tumor. The most commonly



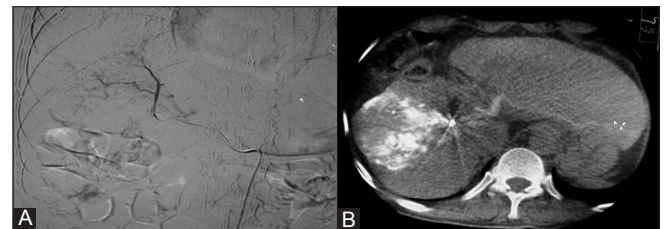
**Figure 1:** Contrast-enhanced computed tomography scan of the liver. Arterial phase image shows (A) hypodense exophytic lesion in segments five and eight of the liver, with minimal enhancement. Venous phase image shows (B) no washout or enhancement of the mass lesion in the portal venous phase



**Figure 3:** Super-selective catheterization of the medial-most branch of the right hepatic artery shows (A) minimal abnormal blush that did not conform to the vascular territory of the tumor; XperCT™ run shows (B) that the catheterized vessel exclusively supplies the normal uninvolved hepatic parenchyma



**Figure 2:** Selective catheterization of the right hepatic artery shows no abnormal tumor blush



**Figure 4:** Super-selective catheterization of the middle branch of the right hepatic artery shows (A) minimal tumoral blush; XperCT™ confirm the catheterization of the abnormal vessel, which is seen (B) to supply the tumor bed



**Figure 5:** Follow-up contrast-enhanced computed tomography shows almost complete tumor necrosis

used chemotherapeutic drug combination includes doxorubicin, cisplatin, and mitomycin C. Doxorubicin is the most common single agent used. The success of TACE depends on identification of the lesion on DSA; however, due to tumor hypovascularity or irregular enhancement of the cirrhotic parenchyma, the lesions may be missed on DSA.<sup>[5]</sup> DEB TACE is the latest modification of TACE, where the embolization particles are made from polyvinyl alcohol hydrogel that are loaded with doxorubicin. The beads are of varying sizes and lead to lumen occlusion and ischemia. The doxorubicin is gradually released locally; the decreased leakage of drug to the systemic circulation and the longer exposure of tumor cells to the drug result in decreased systemic side effects and increased response.<sup>[6]</sup> As the beads are expensive and permanently embolize the vessel, there is a need to selectively embolize only the tumor vessels.

Typical HCCs are hypervascular during the arterial phase and show washout in the portal venous phase and tumor blush on DSA. Meyer, *et al.*,<sup>[7]</sup> reported the sensitivity and specificity of C-arm CT in detecting hypervascular hepatic tumors to be 97-99% and 79-85%, respectively, compared with biphasic multidetector CT. Hypovascular HCCs are minimally enhanced because of poor arterial blood supply and are hence difficult to detect on DSA as no or only minimal abnormal blush is visible on DSA. Angiograms may give a false tumor blush and there is difficulty in exactly delineating the tumor-feeding vessels with DSA in cases of hypovascular HCC. Cone-beam CT is very helpful in confirming the vascular supply from the feeding vessels. The source beam is conical in shape in contrast to conventional multidetector CT, where the beam is fan shaped. The C-arm rotational run is approximately 240°, and multiple 2D projections are acquired and sent to the workstation for image reconstructions.

MPR and MIP images are visible in any plane when viewing

the vascular supply of the cannulated artery. In our patient however, the use of cone-beam CT prevented embolization of normal vessels showing abnormal blush. Complete embolization of normal-appearing tumoral vessels showing minimal or absent tumoral blush was achieved. Cone-beam CT thus can be used to roadmap the feeding artery of hypovascular tumors. Superselective chemoembolization can be performed successfully and accurately. This technique reduces the number of DSA runs required, thereby reducing the dose requirement. Kim, *et al.*,<sup>[8]</sup> concluded that the CT dose index for C-arm CT for body scans was reduced by 49% using a body phantom compared with multidetector CT (MDCT).

In conclusion, the use of cone-beam CT during TACE helps in selectively embolizing the tumor-feeding vessels, thus sparing uninvolved liver parenchyma and allowing efficient and precise drug delivery to the target area. It is especially useful in hypovascular HCCs in which the tumoral vessels show minimal or no abnormal tumoral blush. It also prevents unnecessary chemoembolization of normal liver parenchyma.

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