

Watershed Hepatocellular Carcinoma – Utility of Cone Beam CT for Transcatheter Therapy and Case Report

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Received date: May 23, 2016; Accepted date: August 02, 2016; Published date: August 10, 2016

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Introduction

Transcatheter arterial chemoembolization (TACE) for unresectable hepatocellular carcinoma (HCC) has shown survival benefit and is widely utilized [1]. In order for TACE to be most effective, the chemoembolic agent should be delivered to the entire volume of the target tumor. Embolization of only a portion of the tumor leaves behind viable tumor cells leading to residual disease and possibly progression of disease. Different portions of a tumor may receive arterial supply from separate and potentially remote arterial branches, leading to technical challenges in transarterial therapy. Watershed HCCs, those tumors bridging two or more Couinaud liver segments, commonly receive vascular supply from two or more segmental hepatic arteries regardless of tumor size [2]. Consequently, compared to non-watershed HCC, watershed tumors have lower rates of complete response (CR) [3], and higher rates of local progression [4], after TACE. These suboptimal results are at least partially attributable to incomplete treatment, i.e. not embolizing one or more of the tumor-feeding arterial branches during TACE.

Watershed HCCs along Cantlie's line, the vertical plane along the middle hepatic vein dividing the anatomic right and left lobes of the liver, deserve special mention as they may have feeding vessels arising from the right, left and/or middle hepatic arteries. Chou, et al. [5] reported a residual disease rate of 52.2% for HCC along Cantlie's line treated with unilateral chemoembolization compared with 11.1% after bilateral chemoembolization. These tumors therefore warrant a high index of suspicion for feeding vessels arising from both lobar hepatic artery branches.

Intraprocedural C-arm cone beam CT (CBCT) has become widely used in various interventional procedures including TACE [6,7], with a role complementary to projectional digital subtraction angiography (DSA). Tognolini et al. found that CBCT provided additional information not apparent on DSA in 30% of TACE procedures [6]. Benefits of CBCT include detection of tumors occult on DSA or cross sectional imaging [8,9], lesion characterization to allow differentiation between HCC and pseudo tumors such as arterioportal shunts [10], cross-sectional and/or 3D mapping of tumor arterial supply and non-target arteries [11,12], and monitoring of embolic distribution and geographic tumor coverage after embolization [13].

In the setting of watershed HCC, CBCT is particularly useful for tumor targeting (i.e. mapping of arterial supply) and treatment monitoring (i.e. assessment of the extent of tumor coverage after embolization). Intrahepatic arteries in cirrhotic patients are often extremely tortuous and projectional vessel overlap may be unavoidable with DSA alone. Multiprojectional DSA is often required to delineate tumor-feeding branches and their origins; this can be time consuming,

requires additional intravascular contrast, and increases radiation exposure to the patient and staff. Contrast-enhanced CBCT performed with injection from the common or proper hepatic artery provides a map of the entire hepatic arterial tree, potentially simplifying tumor targeting. Non-contrast CBCT obtained at the completion of TACE depicts retained contrast or lipiodol within the tumor and importantly, along the tumor margin. The extent of geographic contrast saturation of the tumor and tumor margin has been shown to accurately predict tumor response at one month follow up by cross-sectional imaging [14]. Kalb et al. [15], showed that MR enhancement pattern one month after TACE accurately predicts residual disease at six months. Therefore tumor geographic and marginal contrast saturation on non-contrast CBCT obtained at the completion of TACE can serve as a reasonable predictor of short-term tumor response. Furthermore, Miyayama et al. found a statistically significant improvement in technical success and reduction in local recurrence rate with CBCT monitoring of the embolized area during TACE compared to DSA alone [16].

The following case illustrates the utility of CBCT for intraprocedural monitoring during drug-eluting bead TACE (DEB-TACE). Exemption was obtained from our Institutional Review Board for this case report. All data were handled in a manner compliant with the Health Insurance Portability and Accountability Act (HIPAA).

Case

A 66 year old male with alcohol-induced cirrhosis presented with a 3.9 cm liver mass bridging segments IVA/VIII with imaging features consistent with HCC (Figure 1).

The patient was discussed at institutional multidisciplinary liver tumor board. Underlying portal hypertension precluded resection, so selective TACE with doxorubicin-eluting embolic particles was planned. The procedure was performed in a single plane digital angiography suite with a flat panel detector and CBCT capabilities (Allura Xper FD 20; Philips, Hamburg, Germany). After catheterization of the artery to segment VIII, the tumor-feeding vessel was selected and, after confirmatory angiography (Figures 2a and 2b), DEB-TACE was performed. 1 vial of 70-150 µM doxorubicin-loaded drug eluting particles (LC Bead M1[®]; Biocompatibles UK Ltd., Farnham, UK) loaded with 75 mg of doxorubicin diluted to 10 mL in Iodixanol 320 (Visipaque[®]; GE Healthcare, Waukesha, WI) was administered. Per institutional practice, no further embolic was administered. Completion non-contrast CBCT was performed, demonstrating contrast saturation of approximately 50% of the tumor (Figure 2c). The procedure was terminated at this point with plans to

have the patient return for a second TACE procedure to treat the segment IV portion of the tumor. The patient recovered uneventfully.



Figure 1: Pre-treatment contrast-enhanced portal venous phase MRI. Well-circumscribed 3.9 cm tumor in segment IVA/VIII with washout appearance is consistent with HCC (thick arrow). The tumor lies along Cantlie's line straddling the middle hepatic vein (thin arrow).

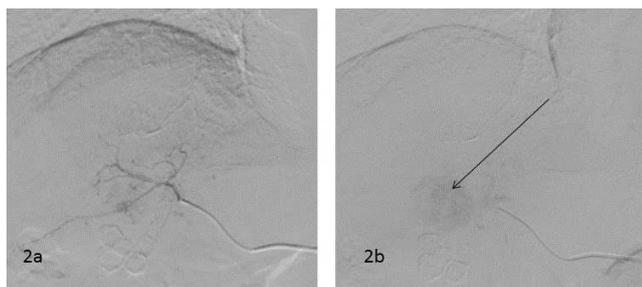


Figure 2: DEB-TACE. Subselective angiography of the segment VIII tumor-feeding artery. (a) Distorted tumor vasculature and early tumor staining are demonstrated on early phase angiographic image. (b) A dense, round tumor stain (arrow) is visible on later phase image.



Figure 2c: Completion non-contrast CBCT during DEB-TACE via the segment VIII hepatic artery. There is contrast saturation of the posterior portion of the target tumor and tumor margin (black arrow) corresponding to that portion of the HCC within segment VIII. No contrast saturation is evident in the anterior portion of the tumor within segment IV (white arrow).

Follow-up contrast-enhanced MRI demonstrated partial response by mRECIST criteria. The non-enhancing treated portion of the tumor corresponded to the tumor volume posterior to the middle hepatic vein within segment VIII (Figure 3) and matched the region of geographic contrast saturation on non-contrast CBCT performed at DEB-TACE (Figure 2c). A second DEB-TACE procedure was performed 2 weeks later. Selective catheterization of the middle hepatic artery revealed tumor enhancement (Figures 4a and 4b) and selective DEB-TACE was performed in a manner similar to that described above. Completion non-contrast CBCT demonstrated contrast saturation of the anterior portion of the target tumor (Figure 5). MRI 1 month later showed complete response by mRECIST criteria (Figure 5).



Figure 3: Follow up portal venous phase contrast-enhanced MRI 1 month after the first DEB-TACE. Non-enhancement of the posterior portion of the tumor within segment VIII (thin arrow) is consistent with treatment response and corresponds to the zone of contrast saturation in Figure 2c. Residual viable tumor with washout appearance is seen in the anterior portion of the tumor within segment IVA (white arrow). The course of the middle hepatic vein (thick black arrow) corresponds to the margin between treated and residual tumor.

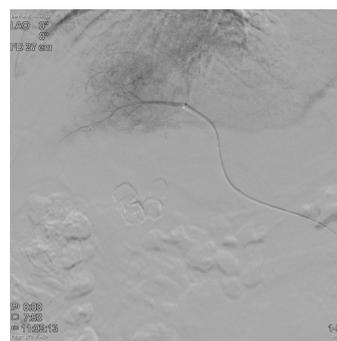


Figure 4a: Repeat DEB-TACE. Subselective arteriography via tumor-feeding vessel arising from the middle hepatic artery. Dense tumor enhancement is evident (arrow).

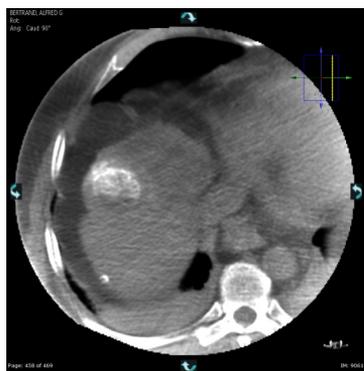


Figure 4b: Completion non-contrast CBCT performed during DEB-TACE via the middle hepatic artery. There is marginal contrast saturation of the anterior portion of the target tumor (white arrow) within segment IV corresponding to the region of residual disease in Figure 3. The posterior, previously treated portion of the tumor is hypoattenuating compared to normal liver parenchyma (black arrow).

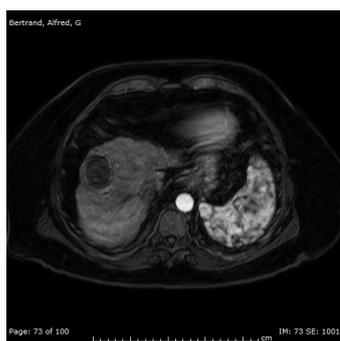


Figure 5: Arterial phase contrast-enhanced MRI one month after second DEB-TACE. There is no residual enhancing tumor tissue, consistent with a complete imaging response by mRECIST criteria.

Conclusion

CBCT is a useful tool for targeting as well as treatment monitoring and confirmation during TACE. The utility of CBCT is especially apparent in the setting of watershed tumors, where blood supply from two or more segmental hepatic arteries is common [3]. Limitations of DSA include poor spatial resolution of overlapping blood vessels and inherent two-dimensionality. In the presented case, the circular tumor enhancement shape by DSA in the anteroposterior projection during the first treatment session (Figure 2) could give the impression that the entire tumor was targeted. CBCT with contrast injection from the common or proper hepatic artery facilitates recognition and targeting of any and all tumor-feeding vessels. Assessment of geographic tumor and tumor margin contrast saturation on non-contrast completion CBCT immediately after embolization serves to confirm treatment of all or a portion of the tumor. In the presented case, completion CBCT performed during the first and second DEB-TACE procedures were complementary and matched the follow-up MRI findings.

In conclusion, watershed tumors along Cantlie's line often receive blood supply from right, left, and/or middle hepatic artery branches regardless of tumor size. Intraprocedural CBCT for targeting and completion monitoring may prompt the operator to seek out and embolize additional tumor feeding vessels, thereby improving the results of TACE. If CBCT is unavailable, selective angiography of both the right and left (and/or middle) hepatic arteries must be performed for identification of all tumor-feeding vessels.

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