Cone-Beam CT Angiography for Hepatocellular Carcinoma: Current Status

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Introduction

Transcatheter arterial chemoembolization (TACE) is the first-line therapy recommended for patients with intermediate hepatocellular carcinoma (HCC) [1–8]. Selective catheterization of a target artery is a prerequisite for achieving effective TACE in HCC patients. However, it is often difficult to determine the relationship between multiple overlapping vessels from 2-dimensional (2D) angiographic images [9–11]. Furthermore, small vessels may be obscured when they are adjacent to large areas of opacification. When complex vascular structures are being imaged, it may be necessary to make multiple acquisitions at various angles to provide adequate visualization. However, multiple acquisitions result in increased radiation exposure to the patient and repeated injections of contrast material. To minimize these angiography risks, it is crucial to provide the operator with a 3-dimensional (3D) representation of the patient’s liver along with its vasculature and lesions.

Over the past decade, interventional radiology (IVR)-CT angiography and cone-beam CT (CBCT) angiography have been introduced as 3D angiography systems. The IVR-CT angiography system consists of angiography and a multidetector row CT (MDCT) unit, and is conducted with the patient on the same bed without risking dislodgment of the catheter [12, 13]. IVR-CT angiography offers high-resolution images of the vascular anatomy or the shape and volume of the vascular territories [14–16]. However, these systems are only found in a lim-
ited number of hospitals because they are rather expensive and require a great deal of space. On the other hand, the CBCT system consists of a C-arm gantry, an X-ray tube and a flat-panel detector (FPD), and can offer great flexibility in orienting the detector around the patient. CBCT is able to provide the benefit of space and time savings while offering good 3D angiography.

This article summarizes the principles, clinical applications and technique of CBCT angiography for HCC treatment.

**CBCT Angiography**

**System**

CBCT mounted on a C-arm was originally performed using an image intensifier system. However, image intensifier systems and charged couple devices suffer from limited spatial resolution. The FPD-based system replaced the image intensifier system during the 1990s. The development of FPD has provided significantly high resolution, high detector quantum efficiency, high frame rate, high dynamic range, small image lag and excellent linearity in comparison with image intensifier detectors [17]. Recent FPDs cover a planar region of 19 × 25 cm and up to 40 × 40 cm for a reconstructed volume of 25 × 25 × 19 cm to 40 × 40 × 40 cm at a high spatial resolution on the order of 150 × 150 μm² pixel size. Furthermore, CBCT allows for lower radiation and intravenous contrast doses by FPD. CBCT imaging is based on a projection acquisition, whereby a cone-shaped X-ray beam and FPD are mounted on a C-arm gantry (fig. 1). This configuration provides projection radiography, fluoroscopy, digital subtraction angiography (DSA) and volumetric CT capabilities in a single patient setup, within the interventional suite. Such capabilities allow the operator to perform intraprocedural volumetric imaging without the need for patient transportation to a CT unit.

The FPD C-arm CBCT data are generated during a rotational sweep of C-arm around the patient. X-ray projection images of the object are acquired in multiple angular directions, following a circular path covering an angular range of at least 200°. The target area is positioned at the center of rotation and CBCT volumes are then obtained by integrating information from the 2D high-resolution projection images.

Generally, the contrast-to-noise ratio of CBCT images is 1.5–2 times lower when compared with that of MDCT, primarily due to less-advanced anti-scatter radiation technology [18, 19]. On the other hand, due to the finer detector pitch, its spatial resolution is superior. This combina-
tion of high spatial resolution and intra-arterial administration of iodinated contrast material compensates for the lower contrast resolution and provides a high-quality tumor depiction along with detailed vascular anatomy.

**Imaging Technique Options**

CBCT has been shown to be a valuable imaging technique, providing in situ cross-sectional imaging of CT-like quality [20]. The reconstructed 3D DSA images show only the enhanced vascular lumina, and data are stored. Therefore, it is easy to evaluate the morphologic characteristics of the hepatic arteries from multiple views with the use of various reconstruction techniques, such as maximum intensity projection (MIP) and volume rendering [21].

**MIP**

MIP is a specific type of rendering in which the brightest voxel is projected into the 3D image. MIP image allows the differentiation between enhanced vascular structures and non-vascular structures, because the result is a projection of the highest density. CT angiographic applications for which the use of MIP is advantageous include the creation of a vascular map for display by a referring physician and easy visualization of small intraparenchymal branches in an enhancing organ, such as the liver or kidney [22]. In practice, MIP is usually performed interactively with a sliding slab, enabling the radiologist to adjust the window, select the optimal orientation to display each artery and modify the slab thickness. This sliding thin-slab MIP technique has been found to increase sensitivity in the detection of lung nodules and arteriovenous malformations [23, 24].

**Volume Rendering**

Volume rendering can better depict soft tissues and 3D relationships because volume rendering can display a set of data in its entirety. This property allows volume-rendered CT angiograms to provide vessel ‘depth’ and to display multiple overlapping vessels, more effectively excluding the surrounding structures [21, 25]. In addition, volume rendering allows for a color display, which often improves the visualization of complex anatomies and 3D relationships. Small vessels are more accurately depicted with volume rendering, and MIP may not be. Recently, the medical imaging community has embraced volume rendering for a wide variety of 3D imaging applications including this navigation imaging on CBCT.

**Tracking Navigation Imaging**

The tracking navigation software is an advanced vascular 3D clinical analysis tool using data from CBCT angiography [26]. There are 2 software programs (Flight Plan for Liver, GE Healthcare, Chalfont St Giles, England, or EmboGuide, Philips Healthcare, Best, The Netherlands), and these 3D navigation tools can automatically depict all vessels in the vicinity of the target as being feeding arteries (fig. 2). Tracking navigation imaging can highlight all vessels (from the tip of the microcatheter to the tumor) that appeared to feed the tumor by coming into close geometric proximity with the region of interest. Moreover, virtual ‘3D roadmap’ imaging can superimpose the live fluoroscopic images with 3D reconstruction in the GE system. The 3D roadmap is automatically adjusted in real time for all changes in C-arm angu-
lations, field of view and table positions. The operator can move the C-arm into an optimal position that best facilitates catheterization and minimizes vessel overlap and foreshortening, without losing the matching between live fluoroscopy and the angiographic roadmap.

**Clinical Outcomes**

Special information about the feeding vessels of HCC is helpful for successful catheterization and sufficient TACE. Kakeda et al. [27] reported that CBCT provided additional useful information in 42 of the 52 lesions (81%) for therapeutic decision making or TACE compared with DSA. Miyayama et al. [28] showed that the sensitivity of CBCT in the detection of the tumor-feeding artery is superior to that of non-selective DSA (81 vs. 38%, p < 0.01).

The availability of CBCT volumetric information can be used to achieve comprehensive visualization of the hepatic arterial anatomy and tumor feeding arteries and to determine the degree of selectivity of drug delivery to the targeted tumors, thus reducing the risk of non-target embolization and potential complications.

Recent developments in software programming have enabled automatic identification of the feeding vessels on 3D angiography. The TACE procedure can be carried out completely in patients with complicated vessels of the liver by color coding the feeding vessels. Miyayama et al. [28] reported on automatic feeder vessel detection software with a true-positive ratio of 88% in identifying the tumor feeding artery. Iwazawa et al. [29] also showed that the sensitivity in detecting tumor feeders was 87.7%. Therefore, automatic computed analysis software is able to achieve greater than 90% sensitivity in tumor feeding artery detection of hypervascular HCC lesions, which is 29–50% higher than visual identification on a nonselective DSA study [26, 30–33]. Automated software may also be used to detect parasitic feeding artery from other than the proper hepatic artery and the cystic artery and select the optimal microcatheter position for drug delivery to avoid non-target embolization [34] (fig. 3).

Unenhanced CBCT after conventional TACE is known as Lip-CBCT, and Lip-CBCT is a technique used to assess the lipiodol deposition in the tumor after conventional TACE. Lip-CBCT imaging provides immediate feedback to the operator with lipiodol conspicuity equivalent to unenhanced MDCT and is predictive of tumor response when compared with 1-month follow-up multiphasic MDCT or contrast-enhanced MRI [31, 35, 36]. The use of Lip-CBCT helps to achieve complete iodized oil filling of HCCs, and therefore improves therapeutic effects by optimizing the embolization end point [36]. Intraprocedural Lip-CBCT depicts HCC with 100% sensitivity compared with preprocedural diagnostic imaging [31].
iodized oil accumulation on Lip-CBCT may be an unfavorable predictor in HCC patients treated with conventional TACE.

Conclusion

C-arm CBCT is an exciting technology with the potential to significantly impact the practice of IVR. CBCT angiography is capable of providing more information than the standard 2D angiography in visualizing HCCs and targeting tumors though precise microcatheter placement in close proximity to HCCs. It can also be useful in evaluating treatment success at the time of the procedure. CBCT is based on immediate feedback to the angiographic procedure. Therefore, CBCT can inspire greater confidence and should be useful for TACE in HCC patients with complicated feeding arteries.

Disclosure Statement

The authors declare that no conflict of interest exists.

References


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