





Consensus



Application of Cone-beam Computed Tomography in Interventional Therapies for Liver Malignancy: A Consensus Statement by the Chinese College of Interventionalists

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Received: June 27, 2024 | Revised: August 25, 2024 | Accepted: August 26, 2024 | Published online: September 12, 2024

Abstract

Despite its crucial role in interventional therapies for liver malignancy, cone-beam computed tomography (CBCT) has not yet been fully integrated into clinical practice due to several complicating factors, including nonstandardized operations and limited recognition of CBCT among interventional radiologists. In response, the Chinese College of Interventionalists has released a consensus statement aimed at standardizing and promoting the application of CBCT in the interventional therapies for liver malignancy. This statement summarizes CBCT scanning techniques, and operational standards, and highlights its potential applications in clinical practice.

Citation of this article: Zhong BY, Jia Z, Zhang W, Liu C, Ying SH, Yan ZP, *et al.* Application of Cone-beam Computed Tomography in Interventional Therapies for Liver Malignancy: A Consensus Statement by the Chinese College of Interventionalists. *J Clin Transl Hepatol* 2024. doi: 10.14218/JCTH.2024.00213.

Introduction

Interventional therapies, such as transarterial chemoembolization (TACE), yttrium-90 selective internal radiation therapy (⁹⁰Y SIRT), and ablation, play a fundamental role in the

management of liver malignancy.¹⁻⁴ These procedures are typically performed under imaging guidance provided by digital subtraction angiography (DSA), computed tomography (CT), ultrasonography, or magnetic resonance imaging (MRI). However, each of these modalities has its limitations. For example, DSA shows blood vessels and tumor staining in 2D images, which may not be sufficient for certain interventional procedures. Ultrasonography offers poor visualization of small lesions and those located near the dome of the diaphragm, while CT does not provide real-time imaging guidance.⁵

Cone-beam computed tomography (CBCT) is a volumetric imaging modality that uses a cone-shaped X-ray beam for scanning.^{6,7} CBCT can be employed for automatic detection and navigation of target vessels, fluoroscopy, and post-TACE assessment of embolization, potentially compensating for some of the limitations of the aforementioned imaging methods. Although the importance of CBCT in interventional therapies for liver malignancy has been recognized, integrating this technique into clinical practice is hindered by several factors, including insufficient recognition by interventional radiologists (IRs), a lack of familiarity with and standardization of parameter applications, and limited areas of application. In response, the Chinese College of Interventionalists has released this consensus statement to standardize and promote the clinical application of CBCT in interventional therapies for liver malignancy.

Methodology

This consensus statement was drafted based on evidence-based medical practices and the authors' clinical experience with CBCT. A comprehensive search was conducted in PubMed, Web of Science, Cochrane Library, Wanfang, and China National Knowledge Infrastructure databases for relevant evidence published from January 2005 to September 2023. The search terms used included: "cone-beam computed tomography"/"cone-beam CT" OR "CBCT" AND "liv-

Keywords: Cone-beam computed tomography; Interventional radiology; Liver malignancy; Consensus statement; Chemoembolization; Ablation.

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er cancer"/"liver malignancy"/"hepatocellular carcinoma"/"intrahepatic cholangiocarcinoma"/"liver metastasis". Articles, systematic reviews, meta-analyses, and clinical studies on the application of CBCT in interventional therapies for liver malignancy were included, while case reports, conference abstracts, and non-English or non-Chinese reports were excluded from the analysis.

The Grading of Recommendations, Assessment, Development, and Evaluations system was used to assess the quality of evidence, categorizing it as high (A), moderate (B), or low/very low (C).^{8,9} The strength of recommendations was classified as strong (1) or weak (2).^{8,9}

Delphi method

We employed the Delphi method to reach expert consensus on recommendations for addressing common issues with insufficient evidence. The Delphi method involved the following steps:

1. Summarize the clinical questions, recommended items, and clinical evidence requiring consensus;
2. Establish an expert group and a writing group;
3. Conduct the first round of expert discussions via email and online meetings to determine the thematic content of the consensus statement and address controversial issues;
4. Hold the second round of expert discussions. During this meeting, the writing group should elaborate on the themes and content of the consensus statement and introduce the consensus items. Experts should discuss the importance of the consensus themes and content, the rationality of the consensus framework and items, the methodology, and the supporting evidence;
5. Conduct the third round of expert discussions online to reassess the rationality and accuracy of the consensus statement, discuss areas needing improvement, and have the writing group make revisions;
6. Hold the fourth round of expert discussions to re-examine the content of the consensus statement and make final recommendations; and
7. Finalize the contents of the consensus statement.

Formulation of consensus statement

Electronic voting was used to gauge expert agreement on the recommendations in the consensus statement. The voting options were as follows: Level A for complete agreement, Level B for agreement with minor modifications, Level C for agreement with major modifications, Level D for neutral, and Level E for disagreement. The percentage of expert agreement was calculated as follows: (number of experts selecting Level A or B) / total number of experts × 100%. If the agreement was less than 75%, experts were re-consulted, and new recommendations were formulated, followed by re-voting to calculate the updated level of agreement. The consensus statement was balanced by considering the following factors: benefits to patients, accessibility and cost-effectiveness of CBCT, patient preferences, and the grade of evidence.

The final consensus statement has been registered on the International Practice Guidelines Registration and Transparency Platform (<http://www.guidelines-registry.cn/index>. Registration number: PREPARE-2023CN980).

Value of CBCT and its scanning protocols

Currently, the main devices used for CBCT include Philips Xper CT (Netherlands), GE Innova CT (USA), Canon LCI (Ja-

pan), and Siemens Dyna CT (Germany). The procedures, scanning parameters, and postprocessing programs used by these systems vary.

CBCT can perform functions that traditional imaging-guided methods cannot, such as displaying and diagnosing tumors and their supplying arteries, including automatic vascular recognition and navigation; providing intraoperative real-time imaging and fluoroscopy; offering precise puncture guidance when used with navigation software; and assessing the degree of embolization immediately after TACE. Therefore, CBCT is an effective imaging guidance technique for interventional therapies used to treat liver malignancy, and its use is recommended in this setting.

CBCT can be used not only to locate tumors but also to accurately delineate tumor blood supply. When using CBCT for 3D scanning of the liver, catheters or microcatheters are typically placed in the hepatic artery or proper hepatic artery. If there are anatomical variations in the hepatic artery, such as the right hepatic artery originating from the superior mesenteric artery or the left hepatic artery originating from the left gastric artery, angiography should be performed first to ensure the acquisition of complete and accurate images. The reconstructed 3D data can then be used for superselective catheterization and to identify the blood-supplying arteries.

Dual-phase or multiphase CBCT scanning modes allow for more accurate identification and differentiation of tumors, better imaging guidance, and a more comprehensive analysis of efficacy compared to other imaging modalities.¹⁰ For these scanning modes, the liver parenchyma filling time during angiography is typically set as the delayed scanning time after the injection of the contrast agent. The contrast agent injection rate is generally one-half or one-third of the angiography rate, and the injection duration is the sum of the filling time and the rotation acquisition time to ensure peak enhancement of the tumor and feeding arteries during scanning. Depending on the equipment, one or more delayed-phase scans can be added to produce contrast-enhanced images of the hepatic arterial phase, portal venous phase, and hepatic venous phase. If all phases need to be displayed simultaneously in a single scan, the injection time should be extended to the venous phase, and the injection rate should be reduced to approximately one-fourth of the angiography rate.

Recommendation 1: CBCT should be used for imaging guidance in interventional procedures to treat liver malignancy. CBCT should be performed by trained professionals following the manufacturer's device instructions (Agreement 100%).

Radiation dose with CBCT

The use of CBCT increases X-ray fluoroscopy time and radiation exposure. Studies have shown that the dose-area product (DAP) generated by CBCT ranges from 17.9 to 18.3 Gy/cm², accounting for 6–13.3% of the total DAP during a TACE procedure. Notably, DAP values can vary depending on TACE procedural conditions, CBCT parameters, and operator proficiency (Level of evidence: B; Recommendation: 1).^{11–13} Studies have indicated that CBCT-guided TACE procedures increase DAP by 2% and operation time by 0.02% compared to non-CBCT-guided TACE procedures. However, other studies suggest that using CBCT during TACE may reduce the need for additional fluoroscopy, thereby mitigating the increase in CBCT-induced DAP (Level of evidence: B; Recommendation: 1).¹² Indeed, the use of high-quality CBCT may

enhance TACE efficiency and reduce the DAP produced by TACE fluoroscopy by up to 46%.¹³

Recommendation 2: Although CBCT increases radiation exposure, its use can effectively reduce the overall radiation dose during TACE procedures (Agreement 94%).

CBCT-assisted detection of tumors during interventional therapies

Gadolinium-ethoxybenzyl diethylenetriamine pentaacetic acid (Gd-EOB-DTPA)-enhanced MRI is generally considered more effective for diagnosing small tumors than conventional gadolinium-enhanced MRI and contrast-enhanced CT. The diagnostic efficacy of Gd-EOB-DTPA-enhanced MRI is superior to that of CBCT (area under the curve: 0.890 vs. 0.681; $P < 0.001$). For hepatocellular carcinoma (HCC) lesions smaller than 1 cm, the sensitivity of CBCT is higher than that of gadoxetic acid-enhanced MRI (90.9% vs. 70.5%; $P = 0.023$), although its positive predictive value is lower (40.8% vs. 57.4%; $P = 0.073$) (Level of evidence: B; Recommendation: 1).¹⁴ Another study demonstrated that dual-phase CBCT was able to identify 93.9% of tumors found by Gd-EOB-DTPA-enhanced MRI (Level of evidence: B; Recommendation: 1).¹⁵ It should be noted that the overall tumor detection rate for CBCT depends on tumor size, the CBCT protocol used, and the defined gold standard. CBCT offers extremely high spatial resolution, especially for lesions smaller than 1 cm, providing advantages that contrast-enhanced CT, contrast-enhanced MRI, and DSA cannot. Some studies have shown that CBCT has higher diagnostic accuracy and sensitivity than CT for diagnosing HCC (Level of evidence: B; Recommendation: 1).^{11,16-19} Due to its accuracy in detecting small lesions, CBCT is particularly useful for identifying lesions missed or not visible on preoperative enhanced CT/MRI, thereby improving treatment efficacy.²⁰ However, the presence of non-tumor enhancing features (e.g., hepatic arterial-venous shunts, abnormal venous drainage, and partial volume effects of enhanced vessels) can reduce the specificity and increase the false-positive rate of CBCT. Therefore, IRs should exercise caution when interpreting CBCT results and selecting potential therapies in the presence of such features.

Although lesions smaller than 1.5 cm may be identified on CT/MRI, they often cannot be clearly visualized on ultrasonography and DSA, making it difficult for IRs to perform percutaneous ablation or TACE. Research has shown that 95% of these lesions can be clearly displayed on CBCT, and 82% of them can be treated by superselective TACE (Level of evidence: B; Recommendation: 1).²¹

Recommendation 3: CBCT should be used during TACE and combined with preoperative imaging to increase the detection rate for small lesions. CBCT can detect malignant tumors that are unclear on CT, MRI, and DSA; however, caution must be exercised to differentiate these tumors from enhancing non-tumor features (Agreement 97%).

CBCT in ablation procedures

CBCT combined with real-time DSA fluoroscopy can serve as an alternative to conventional guidance methods. Percutaneous navigation software based on CBCT 3D reconstructed

images can automatically delineate puncture pathways by determining puncture targets and skin entry points, thereby avoiding important organs preoperatively and minimizing complications related to non-target punctures.^{22,23} Numerous studies have reported the feasibility and effectiveness of various CBCT-guided ablation procedures.^{24,25} For ablation procedures that cannot be guided by ultrasonography, a success rate of 98% is reported when guided by CBCT combined with real-time DSA fluoroscopy (Level of evidence: A; Recommendation: 1).²⁶ Additionally, CBCT-guided sequential TACE ablation therapy is superior to TACE alone for tumors smaller than 5 cm, significantly prolonging progression-free survival (29.0 vs. 19.0 months; $P = 0.019$) (Level of evidence: A; Recommendation: 1).²³ For large HCC tumors, CBCT-guided sequential TACE ablation therapy is also superior to TACE alone, significantly improving tumor response rates (100% vs. 76.7%; $P < 0.05$) (Level of evidence: A; Recommendation: 1).²⁷

Recommendation 4: Performing ablation procedures under CBCT guidance combined with real-time fluoroscopy is an effective supplementary method to conventional imaging-guided methods (Agreement 97%).

CBCT in TACE procedures

Identification and navigation of tumor-feeding arteries

Research has shown that CBCT is more effective than DSA in identifying tumor-feeding arteries, with superior sensitivity (96.9% vs. 77.2%), specificity (97.0% vs. 73.0%), and accuracy (96.9% vs. 75.4%).²⁸ Moreover, the combination of CBCT and DSA can identify more tumor-feeding arteries compared to DSA alone (4.0 ± 1.7 vs. 3.3 ± 1.4 ; $P = 0.003$) (Level of evidence: A; Recommendation: 1).²⁹

CBCT can also be used to navigate feeding vessels with the aid of 3D reconstructed images overlaid onto fluoroscopic images. It can adjust the virtual 3D roadmap when the gantry position changes, allowing IRs to select optimal angles for displaying tumors and their feeding arteries, thus providing guidance for superselective catheterization. Furthermore, numerous vascular recognition and navigation software programs based on CBCT have been developed and successfully applied in clinical settings. These programs can mark the positions of the catheter tip and the target tumor, automatically display the feeding vessels, and highlight the vascular pathway from the catheter tip to the tumor. This technology has a detection rate of up to 90% for segmental tumor-feeding arteries.³⁰⁻³²

Recommendation 5: CBCT can be used to help identify tumor-feeding arteries, and the 3D roadmap generated with CBCT can improve the efficiency and success rate of superselective catheterization of target arteries (Agreement 100%).

Determination of embolization endpoints

CBCT can be used to monitor lipiodol deposition and distribution during conventional TACE (cTACE), enabling IRs to avoid incomplete and non-target embolization due to blind spots in DSA. Research has shown that CBCT is nearly equivalent to conventional CT for monitoring incomplete lipiodol deposition after TACE. The degree of lipiodol deposition is considered

a predictive factor for a complete response. If lipiodol does not entirely cover the tumor, potential collateral arteries need to be identified and thoroughly embolized.^{33,34} Therefore, the endpoint of cTACE can be determined by monitoring lipiodol distribution and deposition using CBCT, which in turn improves both the efficacy and safety of the cTACE procedure.^{33,34}

The non-visualization of drug-eluting microspheres in drug-eluting bead-TACE (DEB-TACE) procedures limits CBCT's ability to monitor their distribution. However, retention of the contrast agent within the tumor can be observed on plain CBCT after DEB-TACE. Plain CBCT can also effectively predict the early response of liver malignancies to DEB-TACE, as the presence of contrast-enhanced high-density residues with clear and complete margins on CBCT is associated with a complete response.^{35,36}

CBCT-based liver parenchymal blood volume (PBV) perfusion imaging can be employed simultaneously for both quantitative and qualitative analyses. This technique highlights tumor vessels in bright colors based on perfusion levels, distinguishing them from embolized tumor vessels. Compared to DSA and plain CBCT, PBV imaging improves residual tumor detection and allows for immediate intraoperative assessment. PBV assessment can be performed both before and after embolization to quantitatively evaluate blood volume within the tumor, comparing residual tumor perfusion levels to accurately assess the embolization effect and minimize residual tumors (Level of evidence: A; Recommendation: 1).^{37,38}

The use of intraoperative CBCT can change the TACE treatment strategy for 19–50% of patients, further optimizing the TACE protocol and improving tumor response and patient survival rates.^{39–41} CBCT-assisted TACE significantly reduces the local recurrence rate of tumors, prolongs overall survival, and increases local progression-free survival (Level of evidence: B; Recommendation: 1).^{35,42}

Recommendation 6: CBCT, PBV perfusion imaging, and other technologies should be used to assist in determining embolization endpoints during TACE procedures (Agreement 97%).

CBCT in ⁹⁰Y SIRT

Identification of tumors, tumor-feeding arteries, high-risk arteries, and abnormal anastomoses

CBCT can be used not only to improve the diagnostic rate for tumors and their feeding arteries but also to identify and locate high-risk arteries. Nontarget embolization of high-risk arteries is the main cause of ⁹⁰Y SIRT-related complications. In a study involving 924 patients, a total of 1,555 extrahepatic arteries originating from the hepatic artery were identified, with CBCT demonstrating a significantly higher identification rate than DSA ($P < 0.05$) (Level of evidence: A; Recommendation: 1).⁴³ In clinical practice, CBCT can help identify high-risk arteries that are not detected by DSA.

CBCT can also be used to identify abnormal anastomoses. Although abnormal anastomoses do not have specific imaging features on CBCT, they can cause abnormal enhancement and may even reveal enhanced small arteries. The presence of these features on CBCT suggests the possibility of abnormal anastomoses, which would require further assessment.

Recommendation 7: CBCT should be used during ⁹⁰Y SIRT to identify tumors and their feeding arteries and to detect high-risk arteries and abnormal anastomoses (Agreement 100%).

Determination of catheter position

CBCT can assist in determining the optimal catheter position. During ⁹⁰Y SIRT, the microcatheter must be placed accurately to treat tumors while minimizing complications. It is crucial to position the microcatheter so that it covers as many tumors as possible while avoiding healthy liver tissue and high-risk arteries. Using enhanced CBCT after positioning the microcatheter allows IRs to assess the number of tumors covered, their feeding arteries, and the potential impact of ⁹⁰Y SIRT on healthy liver tissue (Level of evidence: A; Recommendation: 1).⁴⁴

Recommendation 8: CBCT should be used during ⁹⁰Y SIRT to assist with catheter positioning (Agreement 94%).

Calculation of target liver and tumor volumes

CBCT can be used to calculate the volumes of the target liver and tumors. The prescribed dose of ⁹⁰Y is based on these volumes. CBCT provides a means to calculate these volumes, which enhances the accuracy and safety of ⁹⁰Y SIRT. Studies have shown that CBCT-based calculations of target liver and tumor volumes are more accurate than conventional CT/MRI-based calculations for patients undergoing ⁹⁰Y SIRT (Level of evidence: A; Recommendation: 1).^{45,46}

Recommendation 9: CBCT should be used during ⁹⁰Y SIRT to calculate the volumes of the target liver and tumors (Agreement 97%).

Prospects

While CBCT presents challenges such as limited soft tissue contrast, radiation dose concerns, image artifacts, resolution limitations, and a restricted field of view, its prospects remain promising. Technological advancements, including improved resolution detectors, advanced reconstruction algorithms, and integration with other imaging modalities, are expected to enhance its capabilities. Innovations in radiation dose reduction, real-time imaging, and the incorporation of artificial intelligence will further address current limitations, improving accuracy and safety in interventional therapies for liver malignancies.

Acknowledgments

We thank Megan Griffiths, a scientific writer from Cleveland, Ohio, USA, for her assistance with revising the manuscript.

Funding

None to declare.

Conflict of interest

The authors have no conflict of interests related to this publication.

Author contributions

Consensus statement concept and design (BYZ, ZPY, CFN), drafting the manuscript (BYZ, ZJ, WZ, CL, SHY), literature search (BYZ, ZJ, WZ, CL, SHY), administrative, technical, or material support and study supervision (ZPY, CFN). BYZ, ZJ,

WZ, CL, and SHY are joint junior authors. All authors have read the approved the final version and publication of the manuscript.

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