Comparative study of tumor response between post procedure cone beam computed tomography (CBCT) and follow up triphasic CT/MRI in trans-arterial chemo-embolization (TACE) in patient with hepatocellular carcinoma (HCC)

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Abstract
Background: Early assessment of the effectiveness of TACE is crucial for successful management. Intraprocedural image assessment is important to assess the endpoint of TACE and requirement of additional treatment if needed while the patient is still in the angiography suite.
Aim: To investigate the efficacy of intra-procedure assessment of tumor response compared to follow up triphasic CT/MRI.
Methods: This perspective study was conducted in interventional radiology department, Kasr El-Aini hospital, Cairo University in the period from June 2018 to January 2020 includes 100 adult patients (51 males & 49 females, mean age, 62.7 years ± 7.19 [standard deviation] – 64 first-time TACE) with the diagnosis of HCC (confirmed the typical imaging features of HCC) who underwent TACE using CBCT. Lipiodol retention pattern was assessed at the endpoint of TACE (excellent, moderate, and poor) and correlated with tumor response assessed by modified Response Evaluation Criteria in Solid Tumors (mRECIST) based on follow-up contrast enhanced (CE) computed tomography (CT) or magnetic resonance imaging (MRI) obtained 4–6 weeks post-TACE.
Results: Intra-procedure Lip-CBCT is of significant degree of agreement (P < .001) in assessment of tumor response when correlated with follow up triphasic CT/MRI 4-6 weeks after procedure.
Conclusion: The pattern of lipiodol retention assessed by CBCT can serve as a prognostic indicator of short-term response and could be a reliable intraprocedural monitoring modality during cTACE.

Key words: Hepatocellular carcinoma (HCC)-Transcatheter arterial chemoembolization(TACE)-Barcelona Clinic Liver Cancer(BCLC)-CBCT.

Introduction
Hepatocellular carcinoma (HCC) is the third most common cause of cancer-related death worldwide due to its complexity of tumor pathogenesis, disease recurrence after curative treatment, and metastases. (Vogl, Thomas J. et al. 2019)

Most patients in whom a diagnosis of HCC hepatocellular carcinoma is made have intermediate- or advanced-stage disease. In these patients, local-regional therapies, such as transarterial chemoembolization (TACE), often represent the only therapeutic option according to the official treatment guidelines in both Europe and the United States. (Tacher V et al. 2016)

Visualizing distribution of lipiodol after chemoembolization by fluoroscopy or computed tomography (CT) scan ensures tumor embolization. However, fluoroscopic imaging may fail to detect lack of lipiodol accumulation within the tumor. Computed tomography is more accurate to depict cross-sectional lipiodol distribution, but it is difficult to transfer patients from the angiography suite to the CT suite since the hybrid angiography-CT systems are not always available.

Cone beam computed tomography (CBCT) has been shown to have lipiodol detection rate comparable with multidetector CT imaging. Lipiodol retention with the help of three dimensional quantification software was found to correlate with tumor response in HCC in a recently published paper.

Material and methods

This prospective study was conducted on 100 patients with the diagnosis of HCC who underwent TACE at interventional radiology unit, radiology department, Cairo University Hospitals, from March 2019 to December 2020 and assigned to undergo TACE treatment using DSA then DP-CBCT image navigation.

Inclusion criteria:
1. The diagnosis HCC is confirmed by the typical features of HCC on a dynamic scan.
2. Child-Pugh A to B.
3. BCLC class B.
4. Performance status 0, 1 or 2

Exclusion criteria:
1. Intolerance to the contrast media.
2. Pregnancy or breast feeding.
3. Child-Pugh score >B.
4. Other contraindications to hepatic embolization procedures (e.g. coagulopathy).
5. History of other malignant disease.

- All patients underwent TACE using conventional DSA then three-dimensional image guidance with automatic detection of tumor-feeding vessels computed from DP-CBCT.
Upon completion of TACE, patients underwent a non-contrast-enhanced CBCT (Lip-CBCT) scan for immediate embolization assessment by detection of lipiodol retention within the embolized tumors.

Depending on the pattern of tumor covered by lipiodol, three classes were defined: excellent (more than 90%), moderate (50–90%), and poor (less than 50%).

Correlations between lipiodol retention patterns on Lip-CBCT and tumor response in follow-up contrast enhanced CT/MRI obtained 4–6 weeks post-TACE was assessed.

**Statistical methods**

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA). Data was summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. For comparison of paired measurements within each patient the non-parametric Wilcoxon signed rank test was used (Chan, 2003a). For comparing categorical data, Chi square ($\chi^2$) test was performed. Exact test was used instead when the expected frequency is less than 5 (Chan, 2003b). P-values less than 0.05 were considered as statistically significant.

**Results:**

One hundred patients with Hepato-Cellular Carcinoma underwent Transarterial Chemo-Embolization was included in this study.

The median age of the patients included in the study was 62.5 years old with the number of males was slightly higher than the number of females, contributing to 51% of the study population. All subjects were of Barcelona score B with about 92% Child-Pugh score A and 8% Child-Pugh score B. 64% among them was there first TACE session and about 36% underwent previous TACE. (Table 1)

After removal of the missed cases during follow up, the correlation between post procedure Lip-CBCT and follow up triphasic CT/MRI was done among 85 cases. In Lip-CBCT about 22 patients (25.9%) show excellent response and 63 patients (74.1%) show moderate response, while in follow up triphasic CT/MRI about 20 patients (23.5%) show complete response, 61 patients (71.8%) show partial response and 4 patients (4.7%) show progressive disease. (Table 2)

Correlation between post procedure Lip-CBCT and follow up triphasic CT/MRI revealed significant degree of agreement ($P < .001$) in view of; among the 22 patients assessed as excellent response in Lip-CBCT, from them 20 patients showed complete response and 2 patients showed partial response in follow up triphasic CT/MRI. Also, among the 63 patients assessed as moderate response in Lip-CBCT, from them 59 patients showed partial response and 4 patients showed progressive disease in follow up triphasic CT/MRI. (Table 3)

**Illustrative Case: (Figure 1)**
Clinical Presentation:

A 67-year-old female with hepatitis C cirrhosis complicated by development of right lobe segment VIII HCC focal lesion measuring about 5.5x5cm.

Child Pugh Score: A  BCLC: B

Figure (1): Triphasic CT study shows (a) segment VIII HFL with arterial enhancement, and washout in (b) delayed phase. (c) and (d) DSA through catheterization of replaced right hepatic artery shows tumoral blush at hepatic dome. DP-CBCT was done showing (e) segment VIII HFL with arterial enhancement and washout in (f) delayed venous phase. (g) Non contrast Lip-CBCT shows excellent deposition of lipidol droplets within segment VIII HFL. Follow up triphasic CT 6 weeks after procedure revealed (h) segment VIII well embolized HFL with no arterial enhancement denoting complete response. (I) The lipidol deposition in delayed phase shows the same pattern as Lip-CBCT (g).

In this case DP-CBCT showed high value in post-operative tumor embolization assessment compared to the follow up triphasic CT done 6 weeks later.

Discussion:

Hepatocellular carcinoma (HCC) is the third most common cause of cancer-related death worldwide due to its complexity of tumor pathogenesis, disease recurrence after curative treatment, and metastases. (Vogl, Thomas J. et al. 2019)

Earlier determination of the tumor response after cTACE is essential in decision making for application of additional treatments in patients with HCC.

Imaging techniques, such as 4–6 weeks follow-up contrast-enhanced CT and MR imaging are widely used to evaluate the therapeutic effect.

Regarding intra-procedure assessment of embolized tumors at the end of TACE session, degree of lipidol retention within the tumor was correlated with follow up triphasic CT/MRI one 4 to 6 weeks after procedure which is assessed by mRECIST criteria (the gold standard).

For mRECIST criteria, measurement of enhanced tumor portion rather than the total visible tumor size has been used to evaluate tumor response in HCC patients after cTACE. Based on this post-procedure assessment imaging, a repeat cTACE or tumor ablation would be needed in case there was residual viable tumors were identified.

We studied 85 cases, Lip-CBCT revealed about 22 patients (25.9%) show excellent response and 63 patients (74.1%) show moderate resonse, while in follow up triphasic CT/MRI about 20 patients (23.5%) show complete response, 61 patients (71.8%) show partial response and 4 patients (4.7%) show progressive disease.

Our study showed significant degree of agreement (P < .001) in view of among the 22 patients assessed as excellent response in Lip-CBCT, from them 20 patients showed complete response and 2 patients showed partial response in follow up triphasic CT/MRI. Also, among the 63 patients assessed as moderate response in Lip-CBCT, from them 59 patients showed partial response and 4 patients showed progressive disease in follow up triphasic CT/MRI.
Hu et al. reported similar results after studying 51 hepatic tumors, 40 (78.4 %) had complete response (CR); 8 (15.7 %) had partial response (PR); 1 (2.0 %) had stable disease (SD); and 2 (3.9 %) had progressive disease (PD). The degree of lipiodol retention scored excellent, moderate, and poor, in CBCT images were 39 (76.5 %), 11 (21.5 %), and 1 (2.0 %), respectively.

Chen et al. have reported that CBCT imaging has a similar capability to assess Lipiodol retention as MDCT.

Lip-CBCT failed to tell about progressive cases intra-procedurally compared to follow up triphasic CT/MRI, and it is expected as disease progression needs some time to develop.

Assessing lipiodol retention pattern by CBCT during the cTACE procedure provides near real-time feed-back before the patient leaves the angiography suite and enables the operator to set a more accurate endpoint and perform additional treatment if necessary. (Hu et al., 2018)

**Conclusion**

The pattern of lipiodol retention evaluated by CBCT can serve as a reliable tool and intra-procedural monitoring modality during cTACE.

**Conflict of interest:** No.

**References:**


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- **Bruix j and Sherman M. et al. (2010).** Barcelona Clinic Liver Cancer (BCLC) Staging and Treatment Strategy includes Nexavar for advanced HCC, Conclusions of the Barcelona-EASL Conference, Barcelona, September 2010


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Table 3:

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Figure 1: