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Assessment of automated cone-beam CT vessel identification software during transarterial hepatic embolisation: radiation dose, contrast medium volume, processing time, and operator perspectives compared to digital subtraction angiography

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Abstract

AIM: To evaluate arterial cone-beam computed tomography (A-CBCT) automated analysis software for identification of vessels supplying tumours during transarterial hepatic embolisation (TAE).

MATERIALS AND METHODS: This study was approved by the institutional review board, with waiver of consent. Consecutive TAE procedures using arterial mapping software (AMS), and performed between February 2014 and August 2014, were reviewed. Hepatic arteries were imaged using digital subtraction angiography (DSA) as well as A-CBCT processed with AMS. Interventional radiologists reported (1) potential embolisation target vessels computed using AMS versus DSA alone, (2) modification of the embolisation plan based on AMS, and (3) operator confidence related to technical success. Imaging set-up, processing time, radiation dose, and contrast media volume were recorded.

RESULTS: Thirty of 34 consecutive procedures were evaluated retrospectively. At least one additional embolisation target vessel was identified using AMS in 13 procedures (43%, 95% confidence interval [CI]: 26–61%) and embolisation plan modified in 11 (37%, 95% CI: 19–54%). Radiologists reported AMS increased operator confidence and reduced the number of DSA acquisitions in 25 (83%, 95% CI: 70–97%) and 15 cases (50%, 95% CI: 32–68%), respectively. The average A-CBCT acquisition and processing time was 4 minutes 53 seconds and 3 minutes 45 seconds, respectively. A-CBCT contributed to 11% of the radiation dose and 18% of the contrast media volume

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CONCLUSION: Physicians report increased tumour supplying vessel detection and intraprocedural confidence using AMS during TAE without substantial impact on radiation dose, contrast media volume, and procedure time.

INTRODUCTION

Transarterial hepatic embolisation (TAE) is commonly performed for the treatment of hepatic malignancies and has a demonstrated survival benefit (1). To optimise treatment response and minimise risk during TAE, identification and complete embolisation of tumour vascularity are balanced against preservation of uninvolved hepatic parenchyma (2, 3). Intraprocedural arterial cone-beam computed tomography (A-CBCT) has been shown to improve depiction of tumour vessels and selective delivery of intra-arterial embolic agents, as well as to facilitate identification of digital subtraction angiography (DSA)-occult lesions (4–7). Improved survival has been attributed to the use of A-CBCT for patients with hepatocellular carcinoma (8), although the resources and time required for A-CBCT image acquisition, analysis, and display remain potential barriers to its adoption.

Dedicated arterial mapping software (AMS) providing three-dimensional (3D) reconstructions from A-CBCT imaging has been developed to help identify the course of arteries supplying a hypervascular target region and to facilitate embolisation planning during TAE (9–11). The use of dedicated software has been shown to improve the detection of vessels supplying tumours when compared to conventional DSA or manual CBCT two-dimensional (2D) multiplanar reconstructions (10, 12, 13); however, previous studies have not fully examined the potential impact of A-CBCT vessel segmentation in conjunction with display software from a variety of intraprocedural and operator perspectives.

The aim of this study was to perform a standardised evaluation of an automated A-CBCT arterial mapping software (FlightPlan for Liver, GE Healthcare, Chalfont St Gilles, UK) for relevant vessel detection, procedural efficiency, operator confidence, as well as radiation and contrast dose versus conventional DSA techniques during TAE.

MATERIALS AND METHODS

The present institutional review board approved study comprised 34 consecutive patients with unresectable hypervascular primary or secondary liver tumours undergoing selective bland or drug-eluting bead TAE between February and August 2014 at a single institution. Eight physicians with TAE experience ranging from 5 to 30 years participated in the evaluation. Three radiology technologists trained on the use of AMS participated in the study, with the assistance of an AMS specialist if requested. Procedures were performed using either general anaesthesia with intravenous paralytics and respiratory suspension during A-CBCT acquisition (31 patients) or monitored anaesthesia care (three patients). Breath-holding was synchronised with imaging acquisitions for conscious patients to reduce respiratory motion artefacts.

Image acquisition and display

TAE procedures were performed under fluoroscopic and A-CBCT imaging guidance in three different, but similarly equipped and configured angiography rooms (Innova 4100, GE Healthcare, Chalfont St Giles, UK). Embolisation procedures were performed according to the standard protocol previously described by Brown *et al.* (14). More precisely, the institutional standard imaging workflow (Table 1) consisted in an initial two-dimensional (2D) multi-segment DSA acquired with either manual or power injection of contrast medium into the common hepatic artery (CHA), proper hepatic artery (PHA), or proximal anatomical variant vessel supplying the liver. The DSA imaging parameters consisted in 2 frames per seconds (fps) for 5 seconds, then 1 fps for 5 seconds, and 0.5 fps for the rest of the time. The DSA was followed by A-CBCT with the same catheter position and centred on the anatomical region of interest, and then AMS automatic vascular segmentation. Contrast power injection rates for A-CBCT ranged from 2–4 ml/s. Contrast power injection rates for A-CBCT ranged from 2–4 ml/s and were maintained during the A-CBCT acquisitions for optimal opacification of arterial vasculature. A 4 second delay between initiating the injection and the imaging/rotation was most common. For less vascular tumours, timing delay before A-CBCT imaging was increased based on the initial DSA. The A-CBCT acquisition consisted of a 5 seconds long rotation of the angiography gantry over 192° 3D vascular renderings were generated by the radiology technologist using automated segmentation tools of the AMS and displayed for physicians to formulate an embolisation plan and subsequently superimpose on live 2D fluoroscopy (Innova Vision, GE Healthcare) for planning (Fig. 1). Immediately following the procedure, physicians completed surveys recording their experience with the software (qualitative data collection).

Qualitative data collection

A prospectively designed nine-item questionnaire (Fig. 2) was provided to each interventional radiologist at the conclusion of each procedure to determine whether (1) any target vessels for embolisation identified on the AMS were not suspected on the initial DSA, or vice versa, and (2) the embolisation plan was modified after the AMS analysis. Additional information was collected in each case, including whether (1) the origin of an embolisation target vessel was only visualised on A-CBCT, but not DSA, (2) oblique views (working position outside of anteroposterior to improve vessel origin visualisation) were used for embolisation, and (3) 3D reconstructions were essential for determining the optimal oblique views. Each interventional radiologist reported subjectively whether the AMS and/or 3D planning views contributed to a reduction in the number of DSA acquisitions required during the procedure. Operators were also asked to provide a subjective impression of whether the AMS increased their overall confidence of technical success during the procedure.

Quantitative data collection

The set-up and acquisition time for A-CBCT was recorded and analysed, as well as time from end of acquisition to the AMS output. A-CBCT contribution to the total procedural radiation dose, and relative contribution compared to the initial DSA using the dose-area product (DAP, product of the air kerma at the interventional reference point and the exposed

area) were calculated, as well as contrast media (Omnipaque 300, GE Healthcare) dose for both the A-CBCT and the initial DSA relative to the total contrast medium volume used for the procedure.

Statistical analysis

Results from the questionnaire were expressed as a percentage of the total number of procedures in the study cohort, with 95% confidence intervals (95% CI) computed using the Agresti-Coull method. Quantitative data are presented as averages with standard deviation and range. All statistical analyses were performed with Minitab 16 (Minitab, State College PA, USA).

RESULTS

Thirty-four patients (22 men, mean age 66 years, range 33–86 years; 12 women, mean age 64 years, range 43–79 years) were included in the study. Twenty-one patients had primary liver cancer and 13 had metastasis from an extrahepatic primary malignancy (Table 2), for a total of 56 embolised lesions. Out of 34 consecutive procedures where the AMS was used during the observation period, four were excluded from the analysis for the following reasons: (1) no initial DSA was performed, (2) the target lesion was hypovascular, (3) the post-procedure questionnaire was not properly completed, and (4) vascular imaging could not be analysed due to a large arteriportal shunt. In one patient included in the study, the initial DSA was acquired with contrast medium injected into the PHA, while the A-CBCT was performed after injection of the CHA.

Software evaluation

Physician questionnaire responses and 95% CI are reported in Fig. 3. The AMS contributed to the identification of target vessels not suspected on initial DSA in 13 (43%, 95% CI: 26–61%) cases. One or two additional target vessels were found in eight (61%, 95% CI: 35–88%) and three (23%, 95% CI: 0–46%) of those cases, respectively, while the number of additional vessels was not reported in the remaining two cases. Target vessels identified after AMS analysis resulting in modification of the embolisation plan were embolised successfully in 11 out of those 13 cases (37%, 95% CI: 19–54%). In one case, the additional vessel identified by the AMS could not be catheterised. In the second case, the additional target vessel identified was already occluded from a single embolisation point due to embolic particle reflux. In one case, (3%, 95% CI: 0–10%), a single embolisation target vessel was identified on DSA that was not visualised using the AMS software.

Overall, physicians reported the AMS increased their confidence in 83% (95% CI: 70–97%) of the cases, and reduced the number of DSA acquisitions necessary for TAE in 15 cases (50%, 95% CI: 32–68%).

Radiation dose

The average radiation dose was 198 ± 127 Gy-cm² (range 37–551, 75th percentile 278 Gy-cm²). The average DAP from the initial DSA and A-CBCT were 5.58 ± 3.72 Gy-cm² (range 1.66–17.13), and 18.57 ± 13.60 Gy-cm² (range 5.06–74.28), respectively. The DAP from A-

CBCT accounted for 11% (mean, range 4–34) of the total procedural DAP on average. In the present cohort, the X-ray dose from A-CBCT rotational angiography was approximately equivalent to three initial DSA acquisitions.

Contrast media volume

Approximately twice the volume of intra-arterial contrast media was used to perform the A-CBCT compared to the initial DSA (28.63 ± 5.36 ml, range 18–36 ml, and 13 ± 4.82 ml, range 8–25 ml, respectively). The total volume of contrast medium used during the procedure was 181 ± 65 ml, range 80–320 ml. On average, A-CBCT contributed to 18% (range 6–41) of this total volume.

CBCT acquisition, processing, and analysis time

The average time for A-CBCT setup and imaging was 4 minutes 53 seconds $\pm$ 3 minutes 5 seconds (range 2–12 minutes 20 seconds). The average time for tumour analysis using the AMS was 3 minutes 45 seconds $\pm$ 3 minutes 18 seconds (range 30 seconds to 12 minutes 8 seconds).

DISCUSSION

A-CBCT has been shown to be a valuable tool for hepatic arterial interventions. Wallace *et al.* (4) reported that 3D CBCT vascular imaging impacted catheter-directed hepatic chemoembolisation procedures in 19.2% of the cases studied, and added information without substantial impact in 55.3%. Virmani *et al.* (5) reported that review and analysis of 3D vascular imaging altered catheter position for chemoembolisation in 39% of cases. Both of these studies were performed without the aid of automated vessel detection, segmentation, and vascular pathfinding software.

In several retrospective studies examining the use of automated tumour vessel identification software, detection sensitivity for relevant vessels using the software was higher than for non-automated detection using DSA or 3D images (10, 12, 15–17). In this study, operators reported that the AMS tools facilitated detection of at least one target vessel not suspected on the initial DSA in almost half of the cases and altered the embolisation plan in one-third. These findings are consistent with previous studies evaluating the utility of A-CBCT during hepatic arterial interventions, although with the potential workflow advantage of automated the vessel detection.

In the present study, A-CBCT acquisition, processing and analysis time varied widely, which may be related to tumour vascularity and conspicuity for ROI placement or familiarity with the AMS; however, trained personnel using the AMS can accurately extract and display tumour supplying vessels, with the potential to minimise physician time required for non-automated vessel analysis. The present study suggests that the AMS analysis at the beginning of an embolisation procedure contributes to early detection of relevant target vessels. This knowledge may improve estimation of procedure duration and enable more balanced distribution of prescribed chemotherapeutic doses into multiple vessels when applicable. Additional vessels for hepatic embolisation were discovered using the AMS relative to an initial DSA; however, the present study does not provide conclusive evidence

that those vessels would have been missed otherwise. Target vessels for embolisation may have been seen on DSA performed during or subsequent to embolisation due to vascular flow redistribution.

The use of contrast media and radiation dose associated with A-CBCT imaging were assessed in this study. In a direct comparison, the contrast media injection volume for A-CBCT was nearly twice the volume used in the initial DSA; however, physicians reported that the AMS helped to reduce the number of DSA acquisitions required to complete the TAE in half of the procedures, which may counterbalance the additional contrast media required for A-CBCT. Previously, Iwazawa *et al.* published that the number of angiography acquisitions was reduced from 6.6 to 4.6 times per procedure using tumour supplying vessel detection software (18). With regard to X-ray exposure, a direct comparison again demonstrated a higher dose from A-CBCT relative to DSA. As for contrast media, if use of the AMS lowers the number of DSA acquisitions necessary to complete the procedure, dose reductions may be achievable on that basis. Mean radiation doses after A-CBCT remained below published reference values from the Society of Interventional Radiology (19, 20) for hepatic chemoembolisation (400 and 296.50 Gy-cm² for the reference level and 75th percentile, respectively).

There are several limitations to this single-arm study. First, physician questionnaires, such as those utilised in the present study, are subjective. A robust prospective randomised study might improve upon the validity of results reported here, although randomising the AMS and DSA could be difficult to interpret due to heterogeneity of tumour vascularity across patients. Second, due to the inherent differences between the imaging methods compared in this study (DSA versus A-CBCT with the AMS and 3D planning), there is limited ability to identify the specific factors providing procedural benefit. A comparison of procedures performed with 3D planning only and with addition of the AMS may better characterise the specific role of vessel-detection software. Third, this study broadly demonstrated the potential utility of AMS for relevant vessel detection; however, TAE procedures were not stratified according to specific scenarios in which such software may be most advantageous. Further studies could consider associations with tumour size, shape, location, and type as predictors of an AMS clinical value. Technical limitations of the AMS, related to ROI size selection and vessel segmentation parameters have been reported to impact relevant vessel detection (10, 12, 15, 21), and may have been amplified by real-time use of the AMS during TAE relative to previous retrospective studies.

In conclusion, A-CBCT is known to aid in the identification and catheterisation of arterial vascular supply to hypervascular liver tumours. The present results suggest that dedicated A-CBCT vessel-detection software improves detection of relevant arteries and intraprocedural operator confidence during TAE with acceptable radiation dose levels, contrast media volumes, and image processing time.

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Appendix

Author Contribution:

1. Guarantor of integrity of the entire study: Jeremy Durack, Stephen Solomon
2. Study concepts and design: Jeremy Durack, Karen Brown, Gregoire Avignon, Lynn Brody, Stephen Solomon
3. Literature research: Karen Brown, Jeremy Durack
4. Clinical studies: Jeremy Durack, Karen Brown, Lynn Brody, Constantinos Sofocleous, Joseph Erinjeri, Stephen Solomon
5. Experimental studies/Data analysis: Karen Brown, Jeremy Durack, Gregoire Avignon, Constantinos Sofocleous, Joseph Erinjeri
6. Statistical analysis: Joseph Erinjeri
7. Manuscript preparation: Karen Brown, Jeremy Durack
8. Manuscript editing: Gregoire Avignon, Lynn Brody, Constantinos Sofocleous, Joseph Erinjeri, Stephen Solomon

Declaration of Interests

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Draft questions to be framed on Editorial Manager:

On behalf of all the named authors, I certify that I understand the policy of *Clinical Radiology*. There are no actual or potential conflicts of interest to declare in relation to this article

On behalf of all the named authors, I certify that I understand the policy of *Clinical Radiology*. In accordance with the policy, I wish to declare the following real or apparent conflicts which concern this article:

Gregoire Avignon is a Clinical Research Engineer employed by GE Healthcare. He provided technical expertise regarding the software used in the study. He did not analyze nor interpret the data in this manuscript.

Stephen Solomon has received a research grant from GE Healthcare.

No other authors have conflicts involving the subject matter of the article.

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- Cone-beam computed tomographic arterial mapping improves operator confidence
- Arterial mapping software facilitates identification of tumor supplying vessels
- Cone-beam imaging and arterial mapping software reduce the need for angiography

Figure 1.

AMS workflow during hepatic arterial embolisation procedures. (a) Unprocessed A-CBCT maximum intensity projection. (b) Step 1. Vascular segmentation: the cursor was positioned proximally in the hepatic arterial system to commence automatic vessel extraction. (c) Step 2. Embolisation target definition: a spherical region of interest was positioned over the hypervascular tumour region using 2D cross-sectional images (arrow: region of interest). (d) Step 3. Isolation of relevant arterial vascular supply: automated vessel detection and colour highlighting of arteries supplying the designated hypervascular region of interest. (e) Step 4. Export for live 3D planning display: extracted arterial vasculature transferred to 3D planning software to enable superimposition of the embolisation plan on live fluoroscopy imaging.

Figure 2.

Copy of the prospectively designed questionnaire that was filled in by the physicians at the end of their procedures.

Flight Plan for Liver questionnaire

Questions to the doctor:

N°	Questions	Results	Comments
1	Target vessel identified on the AMS that was not suspected from DSA?	☐ Yes ☐ No	
2	Target vessel identified on DSA that was not target vessel on the AMS?	☐ Yes ☐ No	
3	Did the embolization plan change after the AMS analysis compared to DSA analysis?	☐ Yes ☐ No	
4	Did the embolization plan change after the AMS analysis compared to pre-op imaging?	☐ Yes ☐ No	
5	Did the AMS reduce the number of DSA runs required?	☐ Yes ☐ No	
6	Did the AMS increase the confidence during the procedure?	☐ Yes ☐ No	
7	Target vessel identified on DSA, but vessel origin visible only on A-CBCT	☐ Yes ☐ No	
8	Was oblique view(s) essential to the embolization?	☐ Yes ☐ No	
9	Was the A-CBCT essential for determining the optimal oblique view(s)?	☐ Yes ☐ No	

Glossary:

Target vessel = vessel where catheter is inserted for embolization

Oblique = working position outside of AP.

Figure 3.

Mean and 95% CI for affirmative answers to each physician questionnaire item.

Table 1.

Standard imaging workflow including acquisition, processing, and display.

Workflow sequence	Description
1	DSA imaging performed with an angiographic catheter positioned in the common hepatic artery (CHA), proper hepatic artery (PHA) or proximal anatomical variant vessel supplying the liver. Physicians analysed DSA acquisitions for embolisation target vessel identification.
2	A-CBCT image acquisition. Angiographic catheter injections performed from the same position as the initial DSA.
3	A-CBCT images transferred to the workstation for automated vessel identification by the radiology technologist. Vessel segmentation files saved for subsequent display.
4	AMS results displayed for physician, including 2D multi-planar and 3D views.
5	Display of computed embolisation plan using live planning software. Upon physician request, 2D or 3D roadmaps, 3D volume renderings, or 2D multi-planar reconstructions provided for catheter guidance.
6	Microcatheter advanced into selected target vessel(s).
7	DSA performed to confirm appropriate location for embolisation.

DSA, digital subtraction angiography; 2D, two dimensional; 3D, three dimensional; A-CBCT, automated cone-beam computed tomography.

Table 2.

Biopsy-proven or radiographically diagnosed primary and metastatic malignancies treated by transarterial hepatic embolisation and gender distribution.

Neoplasm	Male	Female
Hepatocellular carcinoma	14	7
Carcinoid	3	2
Kidney	2	
Pancreatic		1
Oesophageal	1	
Gastrointestinal stromal tumour	1	
Bladder	1	
Angiomyolipoma		1
Leiomyosarcoma		1
Total	22	12