



Clinical utility and limitations of tumor-feeder detection software for liver cancer embolization



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ABSTRACT

Purpose: To evaluate the clinical utility and limitations of a computer software program for detecting tumor feeders of hepatocellular carcinoma (HCC) during transarterial chemoembolization (TACE).

Materials and methods: Forty-six patients with 59 HCC nodules underwent nonselective digital subtraction angiography (DSA) and C-arm computed tomography (CT) in the same hepatic artery. C-arm CT data sets were analyzed using the software to identify potential tumor feeders during each TACE session. For DSA analysis, 3 radiologists were independently assigned to identify tumor feeders using the DSA images in a separate session. The sensitivity of the 2 techniques in detecting tumor feeders was compared, with TACE findings as the reference standard. Factors affecting the failure of the software to detect tumor feeders were assessed by univariate and multivariate analyses.

Results: We detected 65 tumor feeders supplying 59 HCC nodules during TACE sessions. The sensitivity of the software to detect tumor feeders was significantly higher than that of the manual assessment using DSA (87.7% vs. 71.8%, $P < 0.001$). Multivariate analysis showed that a tumor feeder diameter of < 1.0 mm (hazard ratio [HR], 56.3; $P = 0.003$) and lipiodol accumulation adjacent to the tumor (HR, 11.4; $P = 0.044$) were the significant predictors for failure to detect tumor feeders.

Conclusion: The software analysis was superior to manual assessment with DSA in detecting tumor feeders during TACE for HCC. However, the capability of the software to detect tumor feeders was limited by vessel caliber and by prior lipiodol accumulation to the tumor.

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1. Introduction

Transarterial chemoembolization (TACE) is an established local therapy for managing unresectable hepatocellular carcinoma (HCC) in patients with advanced cirrhosis [1,2]. Accurate detection of tumor feeders using intraprocedural imaging is indispensable for the technical success of this procedure. Two-dimensional (2D) frontal projection images of digital subtraction angiography (DSA) are used to detect tumor feeders when planning TACE treatment strategies. However, in patients with complex hepatic arterial

vasculature, additional DSA runs in different angles are sometimes required to identify tumor feeders. Such efforts are time consuming and increase exposure to radiation and the use of contrast material.

Recent advances in C-arm cone-beam technologies have enabled the visualization of three-dimensional (3D) vascular anatomy with a single acquisition of C-arm computed tomography (CT) [3]. This technique allows assessment of the arterial vasculature in multiple projections, thereby facilitating an accurate depiction of the tumor feeders along with the target tumor [4–6]. Recently, a tumor-feeder detection software (FlightPlan for Liver; GE Healthcare, Waukesha, WI) was developed for the detection and visualization of potential tumor feeders on volume-rendered C-arm CT images [7–9]. When catheter entry and the target tumor are chosen on multiplanar reformatted (MPR) C-arm CT images, the software automatically provides probable tumor feeders on the workstation screen [7–10]. Pilot studies [7–9] have shown that this software improves the sensitivity of tumor feeder detection with a shorter processing time than that required for manual assessment using DSA. However, approximately 10%

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of tumor feeders were not detected even after using the software.

In this study, we compared the sensitivity of automated analysis using this software with that of manual assessment using DSA for tumor feeder detection, and evaluated factors that affected the ability of the software to detect tumor feeders.

2. Materials and methods

2.1. Patients

Between September 2011 and September 2012, 46 patients (25 men, 21 women; mean age, 72.9 y; range, 38–90 y) underwent selective TACE for HCC using tumor-feeder detection software at Nissay hospital. These 46 patients had 59 HCC nodules (mean size, 17.5 mm; range, 7–38 mm) that were treated with the assistance of the software. Thirty-five patients had single lesions, 9 had 2 lesions each, and 2 had 3 lesions each. Patients with diffuse and infiltrative HCCs were excluded from this study. The study protocol was approved by the Institutional Review Board of our hospital, and written informed consent for the use of the software was obtained from each patient before TACE.

2.2. Chemoembolization

All angiographic procedures were performed by 1 of 2 board-certified interventional radiologists using a flat-panel detector C-arm angiographic system (Innova 3100; GE Healthcare). During each procedure, a 4-Fr catheter was placed into the celiac artery via the femoral artery, and DSA was performed with 20 mL of iopamidol (Iopamiron 370; Bayer Schering Pharma, Osaka, Japan) at a flow rate of 5 mL/s. A 4-Fr catheter or a 2.7-Fr microcatheter (Sniper II; Terumo, Tokyo, Japan) was then advanced into the common or proper hepatic artery. Subsequently, nonselective DSA was performed with 12 mL of iopamidol at a flow rate of 3 mL/s. C-arm CT images of the same hepatic artery were also obtained by injecting 10–15 mL of iopamidol at a flow rate of 1.0–1.5 mL/s. C-arm CT acquisition parameters were as follows: total scanning angle, 200°; rotation speed, 40°/s; acquisition time, 5 s; matrix size, 1500 × 1500; isotropic voxel size, 0.2 mm; and effective field-of-view, 18 cm². Data acquisition was started 7 s after intraarterial injection of contrast material. The volume data sets were automatically transferred to an external workstation (Advantage Workstation 5.0; GE Healthcare). After the target tumor was confirmed using appropriate imaging modalities, 1.7–2.7-Fr microcatheters were advanced into the most probable tumor feeders. A C-arm CT image of the probable tumor feeder was acquired during contrast injection to confirm whether the vessel supplied the target tumor. The feeder vessel was confirmed when the target tumor was enhanced on C-arm CT with reference to the prior CT/MR images. After confirming tumor feeders, the hepatic areas containing target tumors were infused with an appropriate dose of chemotherapeutic agents mixed with lipiodol (Lipiodol Ultrafluid; Terumo, Tokyo, Japan) and embolized with gelatin particles (Gelpart; Nippon Kayaku, Tokyo, Japan) until the tumor vessels were completely filled. Post-procedural C-arm CT images were obtained to ensure that no viable tumors or additional tumor feeders remained. The tumor feeders identified during the TACE session were considered the reference standard in this study.

2.3. Tumor feeder detection using software

Tumor feeders were detected using the software during an angiographic session by a single radiology technologist with more than 30 years of experience in angiographic image acquisition. All image analyses related to tumor feeder detection were performed

on the same commercial workstation (Advantage Workstation 5.0; GE Healthcare). After acquisition of the C-arm CT data, the technologist used a volume-rendered image to determine the catheter entry site. The extraction function of the software was used to extract the entire arterial vasculature as a circumscribed image in approximately 15 s. A circular region-of-interest (ROI) was placed on the 2D-MPR images of the target tumor to cover the entire tumor. The extraction function of the software provided the potential tumor feeders connecting the selected catheter entry to the target region and displayed color-coded images in approximately 30 s. The information obtained during the software analysis of tumor feeders was used for further tumor targeting.

2.4. Tumor feeder detection using DSA

DSA images obtained during contrast injection into the celiac artery and common or proper hepatic artery were evaluated independently by 3 board-certified interventional radiologists, each with more than 10 years of experience in hepatic vascular intervention. To minimize memory bias, all images were evaluated at least 1 month after the final TACE. The DSA images were presented to each observer in random order on a commercial workstation (SYNAPSE; Fujifilm, Tokyo, Japan) by the same presenter, with observers having free access to previous CT/MR images as reference. Observers were blinded to additional angiograms obtained during TACE. All observers were aware about the results of TACE and may therefore have known the exact sites of the tumor feeders during the film reading session. The observers were asked to select and record any possible tumor feeder for each target tumor.

2.5. Image analyses

The interventional radiologist who had participated in all TACE procedures analyzed images using the commercial workstation (SYNAPSE; Fujifilm). Tumor size was measured on axial images of contrast-enhanced C-arm CT, with slice thicknesses of 3 mm, obtained during the TACE session. The diameter of the vessel, relative to that of the nearby catheter tip, was estimated on magnified DSA images and was calculated as arterial size divided by catheter size multiplied by the actual catheter diameter. Tumor vascularity was defined as visibility on DSA and C-arm CT images. Hypervascular tumors were visible on DSA images, whereas hypovascular tumors were difficult to identify on DSA images but visible on C-arm CT images. Tumor location was assessed using the previously obtained CT/MR images. HCC nodules located ≥ 3 cm from the liver capsule were defined as central tumors, whereas nodules located < 3 cm from the capsule were considered peripheral tumors. The reference standard used in this study was the C-arm CT findings of each possible tumor feeder obtained during contrast injection.

2.6. Statistical analyses

The sensitivity and positive predictive value (PPV) of DSA and the software to detect tumor feeder were compared using the McNemar test and the Mann Whitney-U test, respectively. Interobserver variability was assessed using kappa statistics. Interobserver agreement was defined as excellent, fair to good, and poor by kappa values of > 0.75 , 0.40 – 0.75 , and < 0.40 , respectively. Factors associated with detected and undetected tumor feeders were compared using unpaired-*t* tests or Mann Whitney-U tests. Factors affecting the detection of tumor feeders were assessed using univariate analysis. All variables with a *P* value of < 0.1 were entered into multivariate logistic regression analysis with a backward stepwise selection technique. All tests

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