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# The diagnostic advantage of EOB-MR imaging over CT in the detection of liver metastasis in patients with potentially resectable pancreatic cancer

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ABSTRACT

*Background:* Liver metastases (LMs) are sometimes diagnosed intraoperatively, even when multidetector-row computed tomography (MDCT) reveals no LM in the staging of pancreatic cancer (PC). Gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid-enhanced magnetic resonance imaging (EOB-MR imaging) may have a role to play in the detection of LM.

*Methods:* The present study included a total of 201 patients who underwent an EOB-MR imaging examination before undergoing surgical resection for pancreatic cancer that was determined to be radiologically-resectable by MDCT. Intrahepatic lesions that were considered suspected to be liver metastases following an EOB-MR imaging examination were defined as possible lesions (PLs). All PLs were evaluated by a pathological examination or through close follow-up examinations. The diagnostic ability of EOB-MR imaging was assessed. The predictive factors for liver metastasis were evaluated.

*Results:* Thirty-seven PLs were noted in 17 patients: 31 PLs were true LMs, and six were benign lesions (3 hemangiomas and 3 abscesses). Nine LMs were newly detected during surgery and were not detected by preoperative EOB-MR imaging. The diagnostic ability of EOB-MR imaging was as follows: sensitivity, 77.5%; specificity, 94.7%; positive predictive value, 83.8%; negative predictive value, 92.3%; and accuracy, 90.2%. A multivariate analysis revealed that the presence of PL on EOB-MR imaging was the only independent risk factor for intraoperative liver metastasis ($P < 0.001$).

*Conclusion:* EOB-MR imaging was useful in detecting tiny liver metastases from pancreatic cancer in cases that were determined to be radiologically resectable by MDCT.


## Introduction

Among the gastrointestinal malignancies, pancreatic cancer continues to be associated with a poor prognosis due to its low resectability rate. Despite advances in diagnostic techniques, fewer than 20% of patients have localized tumors that are potentially curable at the time of diagnosis [1–3]. Multidetector-row computed tomography (MDCT) is considered to be the most useful imaging modality for diagnosing and staging pancreatic cancer [2,4]. MDCT has the ability to detect the local and distant extent of the tumor. However, liver metastases are sometimes found intraoperatively or after tumor resection within a few months after MDCT.

Gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid-enhanced magnetic resonance (EOB-MR) imaging has a potential role in the detection of liver metastasis. EOB-MR imaging allows clinicians to assess tumor vascularity on hepatic arterial-dominant phase images and enables the acquisition of hepatobiliary-phase images with the uptake of approximately 50% of the gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid by hepatocytes [5,6] EOB-MR imaging has been reported to show good diagnostic ability in patients with hepatocellular carcinoma and colorectal

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liver metastasis [7–12]. Although staging for pancreatic cancer, including liver metastasis has been reported [13–15], the use of EOB-MR imaging in assessing the liver of patients with radiologically resectable pancreatic cancer has not been clarified. The aim of the present study was to evaluate the diagnostic value of EOB-MR imaging in the detection of liver metastasis among patients with pancreatic cancer that was determined to be resectable by MDCT and ultrasonography.

## Methods

### *Patient selection*

Between 2011 and 2015, 257 consecutive patients who were considered to have potentially resectable pancreatic cancer on the basis of MDCT and ultrasonography examinations were scheduled to undergo an EOB-MR examination. In the present study, resectable pancreatic cancer included tumors that were localized in the pancreas and regional lymph nodes without distant metastasis, and which could be removed by pancreatoduodenectomy or distal pancreatectomy with or without combined portal vein resection. Patients who underwent neoadjuvant chemotherapy were excluded from this series [16].

Two hundred and one of the patients who underwent EOB-MR examinations were enrolled in this study and underwent laparotomy with curative intent. The reasons for the absence of EOB-MR imaging were as follows: overscheduling (n = 35), the initial diagnosis of another periampullary tumor (n = 13), implanted metals that were not suitable for MR imaging (n = 5) or claustrophobia (n = 1). No patients underwent preoperative chemo- or chemoradiotherapy, or a laparoscopic evaluation, regardless of the EOB-MR imaging findings during the study period. The demographic characteristics, including the age, gender, tumor location, tumor diameter, and tumor markers including carcinoembryonic antigen [CEA] and carbohydrate antigen 19–9 [CA19-9], were collected from the prospectively collected patients' medical records. The study protocol was approved by the institutional review board of Shizuoka Cancer Center.

### *MDCT imaging*

MDCT scans were performed with a quadruple phase 320-row multi-detector scanner (Aquilion; Toshiba Medical Systems Co, Ltd, Tokyo, Japan). The scanning parameters were as follows: slice thickness, 1 mm; interval, 1 mm (0.5 mm overlap); rotation time, 0.5 s; tube voltage, 120 kV (peak); and tube current, 350–400 mA. The images were obtained after the intravenous administration of 150 ml of 350 mgI/ml iopamidol (Iopamiron; Nihon Schering Co, Ltd, Tokyo, Japan) using a calibrated power injector (Auto Enhance A- 50; Nemoto Kyorindo, Tokyo, Japan) at a rate of 4 ml/s. The early and late arterial phase, portal phase and delayed phase were started at 25 s, 40 s, 70 s, 180 s, respectively, after the injection.

### *MR imaging*

All of the MR examinations were performed using a 3.0-T system (Achieva 3.0T dStream; Royal Philips Healthcare, Amsterdam, Netherlands). For signal reception in all examinations, an anteroposterior phased-array surface coil (32-channel) was placed around the individual to cover the entire liver. Unenhanced T1-weighted imaging including the in-phase and out-of-phase was performed in all patients. T2-weighted imaging with fat suppression, a heavily T2-weighted FSE sequence, and diffusion-weighted imaging was also performed after the dynamic study. During the dynamic study, each patient was given 0.025 mmol/kg (0.1 ml/kg) of Gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid as an intravenous bolus using a power injector (Sonic Shot GX; Nemoto Kyorindo, Tokyo, Japan) at a rate of 1.5 ml/s. A double arterial phase was obtained during a single breath hold, with a scan delay of 30 s for the early arterial phase and 70 s for the late arterial phase, followed by the portal venous phase, which was acquired at 120 s. After the dynamic study, hepatobiliary phase imaging was obtained (15 min after the injection).

### *Imaging analysis*

The imaging evaluations were performed by blinded radiologists who were not involved in the clinical investigation. Lesions were judged as cysts when they were not enhanced after the administration of contrast material and were sharply defined with a homogeneously high signal intensity, similar to that of cerebrospinal fluid, on heavily T2-weighted images. Lesions were judged as hemangiomas when they showed high signal intensity on T2-weighted images, including dot-like enhancement with subsequent contrast material filling or typical imaging findings of hemangioma on dynamic MDCT images [17–19]. After excluding of cysts and hemangioma on EOB-MR images, all other intrahepatic lesions with or without enhancement that were detected by the hepato-biliary phase of EOB-MR imaging were defined as possible lesions (PLs) (Fig. 1).

### *Surgery and lesion tracking*

All of the patients underwent laparotomy and all PLs and liver metastases were checked by inspection, palpation, and intraoperative ultrasonography. Pathological confirmation was also conducted when possible. With the exception of obvious cysts, mass lesions in the liver were confirmed by pathological examination as possible. Nodules on the surface of the liver were resected. Nodules deep in the liver parenchyma were examined by needle biopsy. When three or more nodules were identified intraoperatively, at least two typical nodules were examined and the other nodules were regarded as the same as the pathologically diagnosed lesions. When unresectable lesions, such as liver metastases or peritoneal dissemination, were not detected, pancreatoduodenectomy or distal pancreatectomy with regional lymphadenectomy was performed. All resected patients were followed-up after surgery and were checked for early hepatic recurrence within four months using MDCT to intraoperatively diagnose unidentified PLs. Patients with unresectable disease on laparotomy underwent biliary bypass and/or gastrojejunostomy as appropriate. After palliative operations, patients were also checked for PLs that had not been identified intraoperatively. PLs were judged to be liver metastases when they grew in size over time, to the extent that they became visible on follow-up MDCT. After lesion tracking, all of the PLs and liver metastases were classified into four categories: false-positive, true-positive, false-negative and true-negative. The overall diagnostic ability of EOB-MR imaging was assessed and the risk factors for liver metastasis were analyzed.

### *Statistical analysis*

All of the statistical analyses were performed using the Statistical Package for the Social Sciences software program (version 21.0J, IBM Japan Inc., Tokyo, Japan). Some of the continuous variables were expressed as medians with ranges and compared using the Mann-Whitney U test. Categorical variables and some of the continuous variables were dichotomized by reference to the median values and compared using Fisher's exact test, as appropriate. Univariate and multivariate analyses were performed to determine

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