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Artificial Intelligence Surgery

Review

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Artificial intelligence-based technology for enhancing the quality of simulation, navigation, and outcome prediction for hepatectomy

Hiroji Shinkawa, Takeaki Ishizawa

Department of Hepatobiliary-Pancreatic Surgery, Osaka Metropolitan University Graduate School of Medicine, Osaka 545-0051, Japan.

Correspondence to: Hiroji Shinkawa, M.D., Ph.D., Department of Hepatobiliary-Pancreatic Surgery, Osaka Metropolitan University Graduate School of Medicine, 1-4-3 Asahimachi, Abenoku, Osaka 545-0051, Japan. E-mail: hirojishinkawa9876@gmail.com

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Abstract

In the past decade, artificial intelligence (AI)-based technology has been applied to develop a simulation and navigation system and a model for predicting surgical outcomes in hepatobiliary surgery. To identify the intrahepatic vascular structure and accurate liver segmentation and volumetry, AI technology has been applied in three-dimensional (3D) simulation software. Recently, 3D and 4D printing have been used as innovative technologies for tissue and organ fabrication, medical education, and preoperative planning. AI can empower 3D and 4D printing technologies. Attempts have been made to use AI technology in augmented reality for navigating and performing intraoperative ultrasound. To predict surgical outcomes and postoperative early recurrence in patients with hepatocellular carcinoma, a deep learning model can be useful. Indocyanine green fluorescence imaging is used in hepatobiliary surgery to visualize the anatomy of the bile duct, hepatic tumors, and hepatic segmental areas. AI technology was applied to fuse intraoperative near-infrared fluorescence and visible images. Preoperative simulation, intraoperative navigation, and models to predict surgical outcomes using AI technology can be clinically applied in hepatobiliary surgery. As shown in reliable and robust clinical studies, AI can be a useful tool in clinical practice to improve the safety and efficacy of hepatobiliary surgery.

Keywords: Artificial intelligence, hepatobiliary surgery, indocyanine green, preoperative imaging

INTRODUCTION

The advancement of artificial intelligence (AI)-based technologies in medicine is progressing rapidly. The concept of AI was introduced as a computer program to simulate human cognitive functions. Machine learning is at the core of AI, and deep learning is an important branch of machine learning [Figure 1]. In hepatobiliary surgery, AI technology using a large number of medical images has recently been applied to develop a simulation and navigation system and a model for predicting surgical outcomes[1][Figure 2]. Three-dimensional (3D) reconstruction based on computed tomography (CT) images are used to calculate future liver remnant volume[2]. AI technology can contribute to the development of 3D reconstruction systems[3,4] and perform liver segmentation, Couinaud segmentation, tumor segmentation, and volumetry[5-8]. AI technology has also been used for augmented reality (AR) navigation systems[9-11]. Three-dimensional printing is an innovative technology for tissue and organ fabrication, medical education, and preoperative planning. Recently, 4D printing has emerged, with the fourth dimension being the time-dependent change in shape after printing. AI-based technology can enhance the accuracy and robustness of 3D- and 4D-printed models. For liver surgery navigation, augmented reality has been applied to provide a semitransparent overlay of the preoperative images of the area of interest, such as liver tumors and vessels[12,13]. Moreover, researchers have attempted to use deep learning to obtain real-time semantic segmentation and improve 3D augmentation[9]. In intraoperative ultrasonography, the use of AI technology can accurately identify focal liver lesions[14]. Several deep learning models have been reported to be useful for predicting postoperative complications and survival outcomes using preoperative medical images[15-17]. The microvascular invasion of hepatocellular carcinoma (HCC) is an indicator of an aggressive tumor, tumor recurrence, and poor survival after surgery. Deep learning-based AI using preoperative CT can predict microvascular invasion and survival outcomes[18,19].

Intraoperative fluorescence imaging with indocyanine green (ICG) is used to visualize cancerous tissues and anatomic structures[20]. Recently, it was discovered that using signal acquisition and processing technology, the near-infrared fluorescence signal emitted from ICG can be fused with visible light color images. Convolutional neural network (CNN)-based deep learning models have been broadly applied in image processing and computer vision[21].

In this article, we discuss the application of AI-based technology in developing a simulation and navigation, and prediction model for a surgical outcomes system based on preoperative imaging and ICG in hepatobiliary surgery.

APPLICATION OF AI TECHNOLOGY FOR PREOPERATIVE SIMULATION

AI technology for 3D simulation

The intrahepatic vascular structure and accurate liver segmentation and volumetry must be identified to ensure precise and safe liver surgery[Table 1]. Three-dimensional simulation software has been applied to reconstruct intrahepatic structures and calculate future remnant liver volume[22]. Previous studies using deep learning-based algorithms for the automatic extraction of portal veins and hepatic veins found that the deep learning model contributed to reducing the processing time[3,4]. Chen *et al.* reported that with the use of the residual-dense-attention U-net model, a CNN, accurate segmentation of the liver and liver tumor on CT images could be obtained[5]. Koitka *et al.* demonstrated that a CNN provided fully automated 3D volumetry of the right and left liver on CT images[6]. Mojtahed *et al.* proposed a novel medical software (Hepatica) for performing automatic liver volumetry, followed by semiautomatic delineation of the Couinaud segments[7].

Table 1. Selected studies utilizing AI for preoperative 3D simulation in liver surgery

Reference	AI-based algorithm	Aim	Imagingmodality	Performance
Kazami *et al.*[3]	Deep learning-based algorithm	Extraction of the PV and HV	CT	Dice coefficient for the PV and HV: 0.90 and 0.94 respectively
Takamoto *et al.*[4]	AI-assisted reconstruction	Extraction of the IVC, PV, and HV systems	CT	Shorter processing time compared with the manual method (2.1 min *vs.* 35.0 min, $P < 0.001$)
Chen *et al.*[5]	Residual-Dense-Attention U-Net	Segmentation between liver organs and lesions	CT	Overall computational time reduced by about 28% compared with other convolutions; the accuracy of liver and lesion segmentation: 96% and 94.8% with IoU values and 89.5% and 87% compared with AVGDIST values
Kokita *et al.*[6]	Multi-Resolution U-Net 3D neural networks	Obtain 3D liver volumetry	CT	Sørensen–Dice coefficient: 0.9726 ± 0.0058, 0.9639 ± 0.0088, and 0.9223 ± 0.0187 compared with SoR liver annotation and with right lobe and left lobe annotation
Mojtahed *et al.*[7]	Hepatica: a deep-learning-based liver volume measurement tool	Measurement of segmental liver volume	MRI	Mean Dice score: 0.947 ± 0.010
Lyu *et al.*[8]	CouinaudNet: a system that trains convolutional networks for liver tumor segmentation	Segmentation of liver tumors using Couinaud annotation	CT	Dice per case and overall for tumor segmentation: 62.2% and 74.0% respectively on the MSD08 test set and 68.4% and 80.9% on the LiTS test set

AI: artificial intelligence; CT: computed tomography; 3D: three-dimensional; PV: portal vein; HV: hepatic vein; IVC: inferior vena cava; IoU: intraoperative ultrasonography; LiTS: Liver Tumor Segmentation Benchmark; MRI: magnetic resonance imaging; MSD08: Medical Segmentation Decathlon Task08; PV: portal vein; SoR: standard of reference.

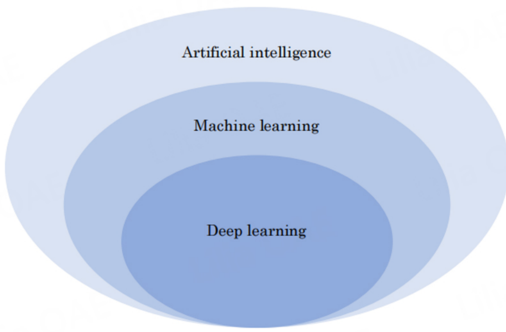

Figure 1. Relationship among artificial intelligence, machine learning, and deep learning.

Preoperative planning	3D volumetry Couinaud segmentation Tumor segmentation 3D and 4D printing
Intraoperative guidance	Augmented reality navigation Assistance in intraoperative ultrasound Fluorescence imaging using indocyanine green
Prediction of surgical outcomes	Postoperative morbidity Tumor recurrence Survival

Figure 2. An overview of artificial intelligence techniques used in preoperative planning, intraoperative guidance, and prediction of surgical outcomes.

CNN can automatically delineate the liver from a 3D T1-weighted magnetic resonance image and segment the volume corresponding to the liver. The new software could accurately delineate the liver and divide the volume into Couinaud segments. Lyu *et al.* used a novel approach to train convolutional networks for liver tumor segmentation using Couinaud segment annotation, which complies relatively better with the radiologists' work practice and significantly reduces manual effort[8]. The new method can use these annotations to estimate pseudo tumor masks as pixel-wise supervision for training a fully supervised tumor segmentation model. AI technology has contributed to the extraction of detailed and precise data on vascular vessels and liver segmental volumes.

AI technology for 3D and 4D printing

Three-dimensional printing is an innovative technology for tissue and organ fabrication, medical education, and preoperative planning. The use of 3D-printed liver models allows surgeons to obtain accurate information regarding vessel anatomy, the relationship between the tumor and vessels, and the parenchymal transection plane. Surgeons can freely handle the patient's liver before surgery. In addition, 3D-printed liver models can be used to train new surgeons[23,24]. Various materials such as polymers and hydrogels are used to fabricate the 3D-printed structure, and a complex creation process, such as the extrusion of feedstock material and building components layer by layer with dimensional accuracy, is needed. Meiabadi *et al.* reported that an artificial neural network-based method can enhance the accuracy of modeling for toughness, part thickness, and production cost-dependent variables[25]. Rojek *et al.* showed the utility of AI-based design for 3D printing in saving materials and reducing waste[26]. Recently, 4D printing has emerged, in which the fourth dimension of time is added to 3D printing, connecting the change of shape, properties, and functionality of the printed material over time following stimuli. An AI algorithm can be used to determine the best design of the toolpath and the stimuli-responsive material distribution, allowing precise shape control of the 4D-printed structure. AI technology can also ameliorate the design of 4D printing using a library of previous scans of the target region of interest and coupling it with incomplete anatomy scan data to reconstruct a patient-specific 4D-printing model. AI-based 4D printing can improve the form and function of the materials in shape- changing and shape memory[27].

APPLICATION OF AI TECHNOLOGY FOR INTRAOPERATIVE NAVIGATION

AI technology for AR and intraoperative ultrasound

Intraoperative navigation techniques, which began with intraoperative ultrasound, may help surgeons perform liver surgery. Recently, AR has been applied to assist the operator in minimally invasive surgery. Liver tumors and vascular and biliary structures reconstructed using preoperative CT images are projected on the liver surface during liver parenchymal transection[28]. Adballah *et al.* used AR software during the laparoscopic resection of liver tumors[29]. Pseudotumor was created in sheep cadaveric liver, and a virtual preoperative 3D model was reconstructed using CT imaging. When the tumor image and 1-cm peritumoral margins were projected onto the liver surface during AR laparoscopic liver resection, the resection margins were more accurate and had less variability than those obtained using standard ultrasonographic navigation. CNN has been used to obtain real-time semantic segmentation of the scene and improve the precision of the subsequent 3D enhancement for an in-vivo robot-assisted radical prostatectomy[9]. Lin *et al.* proposed using a dual-modality endoscopic probe for tissue surface shape reconstruction and hyperspectral imaging enabled by a CNN model[10]. Structured light images are used to recover the depth maps of tissue surfaces using a fully convolutional network. The spectrographic and RGB images were jointly processed by a CNN-based super-resolution model to generate pixel-level dense hypercubes. By combining the depth maps and hypercubes using AR, surgeons can visualize the recovered 3D surfaces, narrow-band images, and oxygen saturation maps. Luo *et al.* evaluated the utility and accuracy of the proposed AR navigation system for performing liver resection by a stereoscopic laparoscope using five modules: hand-eye calibration, preoperative image segmentation, intraoperative liver surface reconstruction, image-to-patient registration, and AR navigation[11]. An automatic CNN-based algorithm was used to segment the liver model using preoperative CT images. An unsupervised CNN framework was introduced to estimate the depth while reconstructing the intraoperative 3D model for registration. AI systems have also been applied in intraoperative ultrasound. Barash *et al.* developed an AI system to detect liver lesions in intraoperative ultrasound. The area under the curve (AUC) of the algorithm performance was 80.2%, and the overall classification accuracy was 74.6%. The algorithm was found to assist in identifying focal liver lesions in intraoperative ultrasound performed by the liver surgeon[14].

AI technology for fluorescence imaging using ICG

ICG is mainly used as a fluorogenic reagent for fluorescence imaging-guided surgery. Protein-bound ICG emits fluorescence that peaks at approximately 840 nm when illuminated with near-infrared light (750 nm-810 nm)[30]. Because it is hard for this wavelength to be absorbed by hemoglobin or water, structures that contain ICG can be visualized through human tissue thicknesses of up to 5 mm-10 mm using a near-infrared camera system. ICG fluorescence imaging is used in hepatobiliary surgery to visualize the anatomy of the bile duct, hepatic tumors, and hepatic segmental areas. Intravenous injection of ICG during surgery allows fluorescence images of the bile ducts to be obtained in the surgical field. Fluorescence cholangiography provides detailed information on the anatomy of the extrahepatic bile duct. At first, fluorescent images of the biliary tract are displayed on a monitor with standard spatial resolution images. Switching from standard images to fluorescence images is required[31]. The high sensitivity of image sensors and advances in signal-processing technology have allowed for the application of fluorescent imaging in laparoscopic surgery[32,33]. Recent advances in imaging technology have enabled the fusion of fluorescence and full-color visible images with high-resolution quality[34] and allowed for the application of fluorescence imaging to laparoscopic liver surgery[35]. In addition, deep learning-based algorithms have been applied to fuse fluorescence images with visible light images. The deep learning fusion method is based on CNNs and can achieve a good infrared and visible image fusion effect[21]. Liu *et al.* used a CNN to obtain a weight map and used image pyramids to fuse infrared and visible images[36]. Zhang *et al.* proposed an adaptive brightness fusion method using the deep learning fusion method to fuse intraoperative near-infrared fluorescence and visible images[21]. Shen *et al.* applied a deep CNN to capture fluorescence imaging to determine glioma quickly and accurately in real-time during surgery. The developed deep CNN combined with the second near-infrared window fluorescence images can predict the pathological diagnosis while achieving an AUC of 0.945 during surgery[37].

The CNN architecture has also been applied to fluorescence lifetime imaging microscopy (FLIM). FLIM is an imaging technique that uses the inherent properties of fluorescent dyes. It identifies different intensity patterns and the lifetime of autofluorescence between cancerous tissues, margins, and normal tissues[38]. CNNs can reduce the acquisition time required to reconstruct pixel raw fluorescence data into intensity and lifetime images[39]. Marden *et al.* reported that a CNN allows for accurate and rapid localization and visualization of aiming beam segmentation during FLIM acquisition[40].

APPLICATION OF AI TECHNOLOGY TO PREDICT SURGICAL OUTCOMES

AI is also being used to predict postoperative morbidity and recurrence after liver surgery [Table 2]. When used as a mathematical tool, an artificial neural network model can predict postoperative liver failure and early recurrence after hepatic resection of HCC[15,16]. In previous reports, AI-based models using the machine learning technique were able to predict postoperative morbidity after liver, pancreatic, and colorectal surgery with a C-statistic value of 0.74[17]. Li *et al.* developed a deep CNN nomogram that predicted microvascular invasion in HCC and survival outcomes including recurrence-free survival and overall survival based on contrast-enhanced CT image and clinical variables[19]. The AUC value was 0.897 in the validation cohort. Wakiya *et al.* reported the use of a deep learning model to predict early postoperative recurrence after resection of intrahepatic cholangiocarcinoma using plain CT imaging from 41 patients. The

Table 2. AI technology to predict surgical outcomes in patients with hepatocellular carcinoma

Reference	AI-based algorithm	Predicted object	Incorporated variables	Performance
Mai *et al.*[15]	ANN model	Post-hepatectomy early recurrence (within two years)	γ-GTP, AFP, tumor size, tumor differentiation, MVI, satellite nodules, and blood loss	AUC: 0.753 in the derivation cohort and 0.736 in the validation cohort
Mai *et al.*[16]	ANN model	Postoperative severe liver failure[#]	Plt, PT, T-Bil, AST, standardized future liver remnant	AUC: 0.880 in the development set and 0.876 in the validation set
Li *et al.*[19]	DCNN	Microvascular invasion, DFS, and OS	Clinicoradiologic features	AUC of DCNN nomogram: 0.929 in the training cohort and 0.865 in the validation cohort; the DFS and OS differed significantly between the DCNN-nomogram-predicted groups with and without MVI
Our data (unpublished)	AI model implemented using CNNs and multilayer perception as a classifier	Postoperative complications of Clavien-Dindo classification II or higher and intraoperative blood loss	Arterial preoperative CECT imaging phase, sex, age, body mass index, preoperative ASA physical status classification, diabetes mellitus, serum ALT, Child-Pugh classification, Plt, and laparoscopic approach	AUC: 0.71 for postoperative complications and 0.83 for major blood loss

AI: artificial intelligence; ANN: artificial neural network; AFP: alpha-fetoprotein; AUC: area under the curve; ASA: American Society of Anesthesiologists; ALT: alanine transaminase; AST: aspartate aminotransferase; CNNs: convolutional neural networks; CECT: contrast-enhanced computed tomography; DCNN: deep convolutional neural network; DFS: disease-free survival; γ-GTP: γ-glutamyl transpeptidase; MVI: microvascular invasion; OS: overall survival; Plt: platelet count; PT: prothrombin time; T-Bil: total bilirubin.
[#]Grades B and C as defined by the International Study Group for Liver Surgery.

average sensitivity, specificity, and accuracy were 97.8%, 94.0%, and 96.5%, respectively[41].

We have recently developed deep learning models based on contrast-enhanced CT imaging to predict surgical outcomes and postoperative early recurrence in patients undergoing hepatic resection for HCC. The data of 543 patients who underwent initial hepatectomy for HCC were randomly classified into the training, validation, and test datasets in a ratio of 8:1:1. Arterial preoperative contrast-enhanced CT imaging phases and several clinical variables, including sex, age, body mass index, preoperative American Society of Anesthesiologists physical status classification, the presence of diabetes mellitus, serum alanine aminotransferase level, Child-Pugh classification status, platelet count, and laparoscopic approach, were used to create the model for predicting surgical risk. The surgical risk was assessed using intraoperative blood loss and postoperative complications of Clavien-Dindo classification II or higher. The deep learning model predicting both major blood loss and postoperative blood loss was developed using a dense convolutional network with explanatory variables including clinical data and contrast-enhanced CT imaging. To evaluate the predictive performance of differential models, we applied the receiver operating characteristic (ROC) curves and their AUC values. The AUCs of the predictive model for postoperative complications and major blood loss were 0.71 and 0.83, respectively [Figures 3 and 4]. Using the deep learning model, the predicted blood loss was significantly correlated with measured blood loss during hepatic resection [$P < 0.01$; Figure 5].

We developed the predictive model for the early recurrence of HCC by performing a deep learning analysis using a dense convolutional network as a training dataset with explanatory variables, including clinical data and saliency heat maps [Figure 6]. The data of 543 patients who underwent initial hepatectomy for HCC were randomly classified into the training, validation, and test datasets in a ratio of 8:1:1. Arterial preoperative contrast-enhanced CT imaging phases and several clinical variables, including sex, age, serum alanine aminotransferase and alpha-fetoprotein, Child-Pugh classification, and platelet count, were used to develop the predictive model for early HCC recurrence. This study defined postoperative early recurrence as intra- or extrahepatic recurrence of HCC within the first 2 postoperative years. This deep learning model

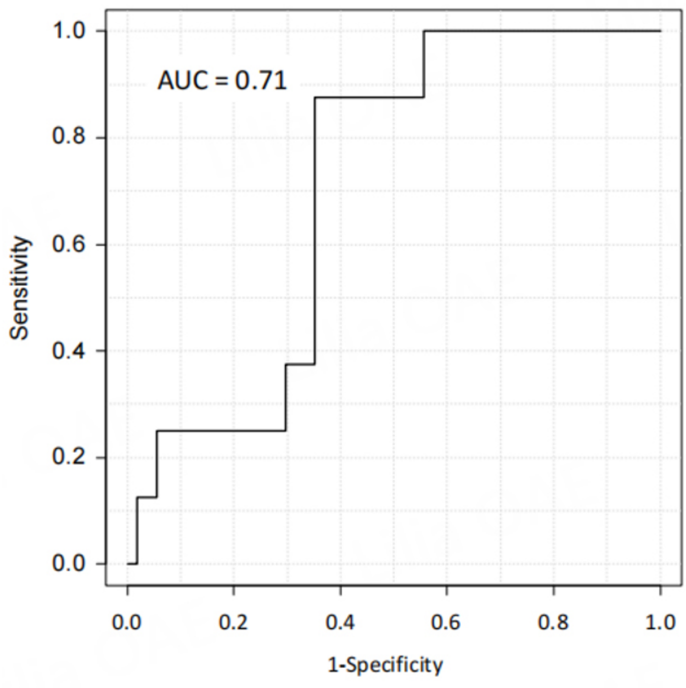

Figure 3. Receiver operating characteristic curve of the deep learning model to predict postoperative complications after hepatic resection of hepatocellular carcinoma with the area under the curve value.

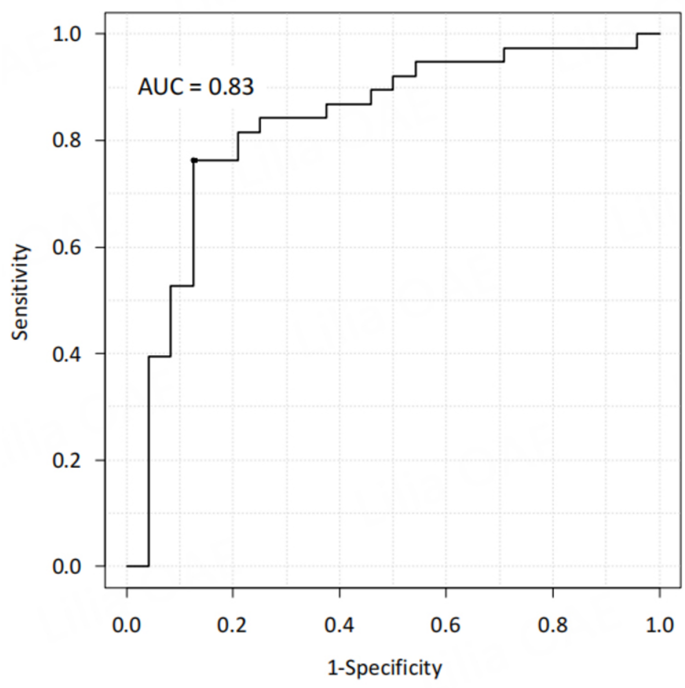

Figure 4. Receiver operating characteristic curve of the deep learning model to predict major blood loss after hepatic resection of hepatocellular carcinoma with the area under the curve value.

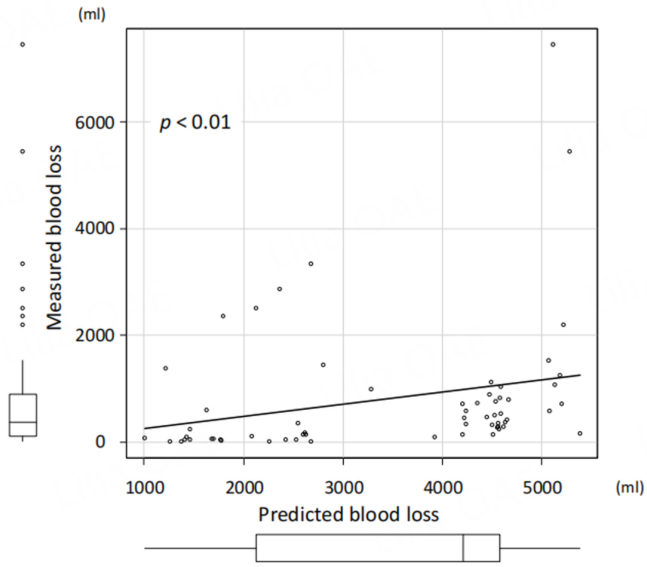

Figure 5. Correlation between predicted blood loss and measured blood loss during hepatic resection of hepatocellular carcinoma.

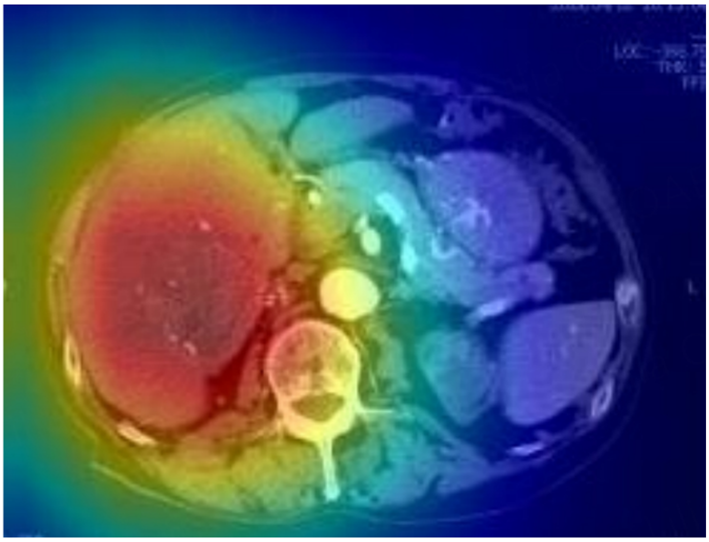

Figure 6. Saliency heat map of representative patients using the deep learning model. The red color highlights the region of interest to predict early recurrence.

demonstrated high accuracy for predicting early recurrence (within 1 year after surgery) by the ROC curve analysis with the area under the ROC curve values of 0.69 in the test dataset and 0.72 in the validation dataset [Figure 7]. Thus, deep learning-based AI using preoperative CT can be useful for predicting the early recurrence of HCC after surgery.

FUTURE PERSPECTIVES

It is hoped that AI will provide better and more individualized planning for each patient undergoing hepatobiliary surgery. In hepatobiliary surgery, significant progress has been made in preoperative simulation, intraoperative navigation, and prediction of surgical outcomes using AI. However, most studies on AI-based technology in hepatobiliary surgery had a retrospective design. Thus, to acquire reliable results, it is desirable to perform future studies on large patient populations collected in a prospective multicenter trial. Through reliable and robust clinical studies, AI can be a useful tool in clinical practice for improving the safety and efficacy of hepatobiliary surgery.

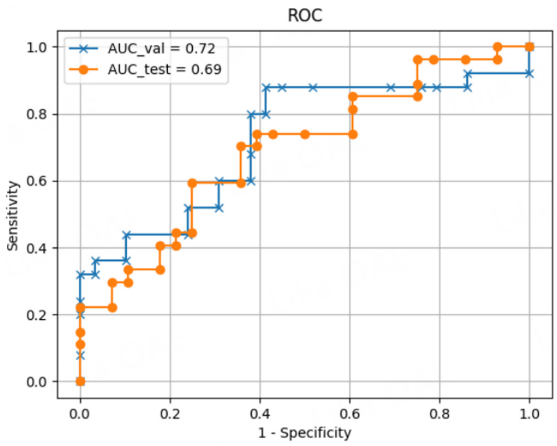

Figure 7. Receiver operating characteristic curve of the deep learning model to predict postoperative early recurrence of hepatocellular carcinoma with the area under the curve value in the test and validation datasets.

DECLARATIONS

Authors' contributions

Made substantial contributions to the conception and design of the study and performed data analysis and interpretation: Shinkawa H, Ishizawa T

Performed data acquisition, as well as providing administrative, technical, and material support: Shinkawa H, Ishizawa T

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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