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ORIGINAL ARTICLE

Binary Classification of Benign and Malignant Hepatic Lesions with Portal Venous Phase Computed Tomography Images with Deep Learning: A Single-institution Study

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Background: Differentiate benign and malignant hepatic lesions with a limited phase of CT scan is a practical clinical challenge. **Aim:** To evaluate the feasibility of differentiation of benign and malignant hepatic lesions with portal venous phase computed tomography (CT) images with deep learning. **Methods:** This was a retrospective single-center study; patients with focal hepatic lesions were detected in the contrast-enhanced CT scan from January 2016 to December 2018 were enrolled. Benign hepatic lesions enrolled in this study include hepatic cysts and hepatic hemangioma; malignant lesions include hepatocellular carcinoma (HCC) and hepatic metastases. Portal venous phase CT images of focal hepatic lesions were labeled by one radiologist with 6-year experience in abdominal radiology. Labeled CT images were input into convolutional neural network (CNN) to perform binary classification with training-test split of 70%:30%. The performance was evaluated by precision, recall, F1-score, and receiver operating characteristic curves. **Results:** There were 214 images of benign hepatic lesions and 223 images of malignant hepatic lesions enrolled in this study, including 84 hemangiomas, 131 hepatic cysts, 146 HCC, and 77 hepatic metastatic lesions. CNN model achieved the best results to classify benign and malignant hepatic lesions, with an average test precision of 0.91, recall of 0.91, and F1-score of 0.91. The area under the curve was 0.96. **Conclusion:** With portal venous phase CT images, CNN can perform binary classification of benign and malignant hepatic lesions with acceptable accuracy in a limited dataset.

Key words: Deep learning, computed tomography images, convolutional neural network

INTRODUCTION

The liver is the largest solid internal organ in the human body. In a study including over 17,000 individuals who underwent screening chest computed tomography (CT),[1] the prevalence rate of incidental hepatobiliary findings was 6%. The hepatic lesions can be categorized into benign and malignant; for malignant lesions, urgent management is of importance in the prevention of disease progression. In the benign hepatic lesions, the reported incidence of hepatic cysts was 17 in 10,000 cases[2] and are encountered in daily clinical practice. Hepatic hemangiomas are the most common benign hepatic tumors with incidence about 2.5%;[3] they are most commonly found in young females, with a female–male ratio of up to 5:1.[4] Hepatocellular carcinoma (HCC) is the most common primary hepatic neoplasm,[5] with relatively high incidence in East and Southeast Asia. For liver metastases, 5.14% of primary cancer patients presented with synchronous liver metastases as confirming diagnosis;[6] among them, the most common primary sites were breast and colorectal cancers.

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In the CT diagnosis of hepatic lesions, multiphasic CT is often required for precise diagnosis. For HCC, typical imaging features include early arterial enhancement and washout in the portal venous or delayed phases; in other words, at least two phases of a CT scan are required for diagnosis. More phases of CT scans indicate higher radiation dose, higher contrast dosage, and higher medical expenditure. In emergent departments and regional institutions, determining whether hepatic lesions need management may be more important than establishing a definite diagnosis. In this scenario, binary classification of benign and malignant hepatic lesions is crucial to decide whether patients should be referred to a specialist or medical center.

Artificial intelligence has been introduced into diagnostic radiology for decades, from widely-used computer-aided diagnosis[7] to cutting-edge deep learning using convolutional neural network (CNN) to detect abnormalities[8] and predict patient survival.[9] There are published researches discussing using multiphasic CT imaging to differentiate focal hepatic lesions.[10,11] However, in certain clinical scenarios, multiphasic CT scan may not be accessible. Thus, to differentiate benign and malignant hepatic lesions with a limited phase of CT scan is a practical clinical challenge.

This study aims to perform binary classification of benign and malignant hepatic lesions with CNN. The classification is worked with portal venous phase CT images, which are the most common contrast-enhanced CT phases performed in clinical scenarios. We assumed that CNN can differentiate benign and malignant hepatic lesions only with single-phase CT images, which may apply to greater applicability.

MATERIALS AND METHODS

Patient population and inclusion/exclusion criteria

This study was approved by the ethical committee (protocol number: TSGHIRB No. 2-108-05-153 approval date: 2019-Oct-02) of our institutional review board and a waiver of informed consent was granted for the radiological report and image review. The study was also in compliance with the Health Insurance Portability and Accountability Act. The patients with hepatic cysts, hepatic hemangiomas, HCCs, and liver metastatic lesions were included. The diagnosis was confirmed by serious imaging follow-up or tissue diagnosis. The portal venous phase images were selected for labeling. The exclusion criteria were (a) those with prominent artifacts in the CT scan, (b) those of hepatic lesions treated with transarterial chemoembolization, systemic therapy, or radiotherapy, (c) those with size below 1.5 cm in maximal diameter, (d) those of hepatic lesions encasing hepatic arteries, portal veins or hepatic veins, and (e) those of hepatic lesions located in the subcapsular region, with part of their border contacting the peritoneal fat, diaphragm, stomach, gallbladder, or kidneys rather than the normal liver parenchyma.

Computed tomography scan

CT examinations were performed with multi-detector row scanners (LightSpeed 16; GE Medical Systems, Milwaukee, WI, Siemens, or Philips Medical Systems, Cleveland, OH, USA). All patients had unenhanced and contrast-enhanced portal venous phase CT scan. Contrast-enhanced images on the portal venous phase were acquired, starting 80 s after bolus injection of intravenous contrast material (2 mL/kg at a rate of 2–3 mL/sec). Patients received 80–120 mL of intravenous iohexol (Omnipaque 350, Nycomed Amersham, Princeton, NJ) before scanning. The dose of injected contrast material was tailored to body weight at the ratio of 1.5 ml/kg weight. Imaging parameters for CT scanning and reconstruction were as follows: beam collimation, 0.5 mm; slice thickness, 5 mm; pitch, 1.5; tube voltage, 120 kV; and a maximum tube current of 230 mA, controlled using dose modulation. The anatomical coverage was from the hepatic dome to the iliac crest. Multiplanar reformation was reconstructed, but not routinely used for interpretation. All the CT images were reviewed on a dedicated picture archiving and communication system workstation.

Imaging labeling

The CT images were output as PNG files from the PASC workstation [Figure 1] with 512 × 512 in size. Manual segmentation was performed by two radiologists with 3 and 8 years of experience in abdominal radiology, respectively. The region of interest (ROI) contained the entire volume of the lesion on the portal venous phase CT images. Labeling was performed on an open-source software platform (Labelme, a graphical image annotation tool, http://labelme.csail.mit.edu). Then, the ROI was resized to 64 × 64 pixels.

Architecture of convolutional neural network

In this study, Python programming language was used for constructing CNN. The CNN comprised several layers, including convolutional layer, ReLu layer, max polling layer, flatten layer, dense layer, and dropout layer [Figure 2]. The CNN architecture implied in this study was based on the reference from the GitHub article.[12] The final layer of CNN was the sigmoid function, which acted as the activation function and will determine the probability of benign or

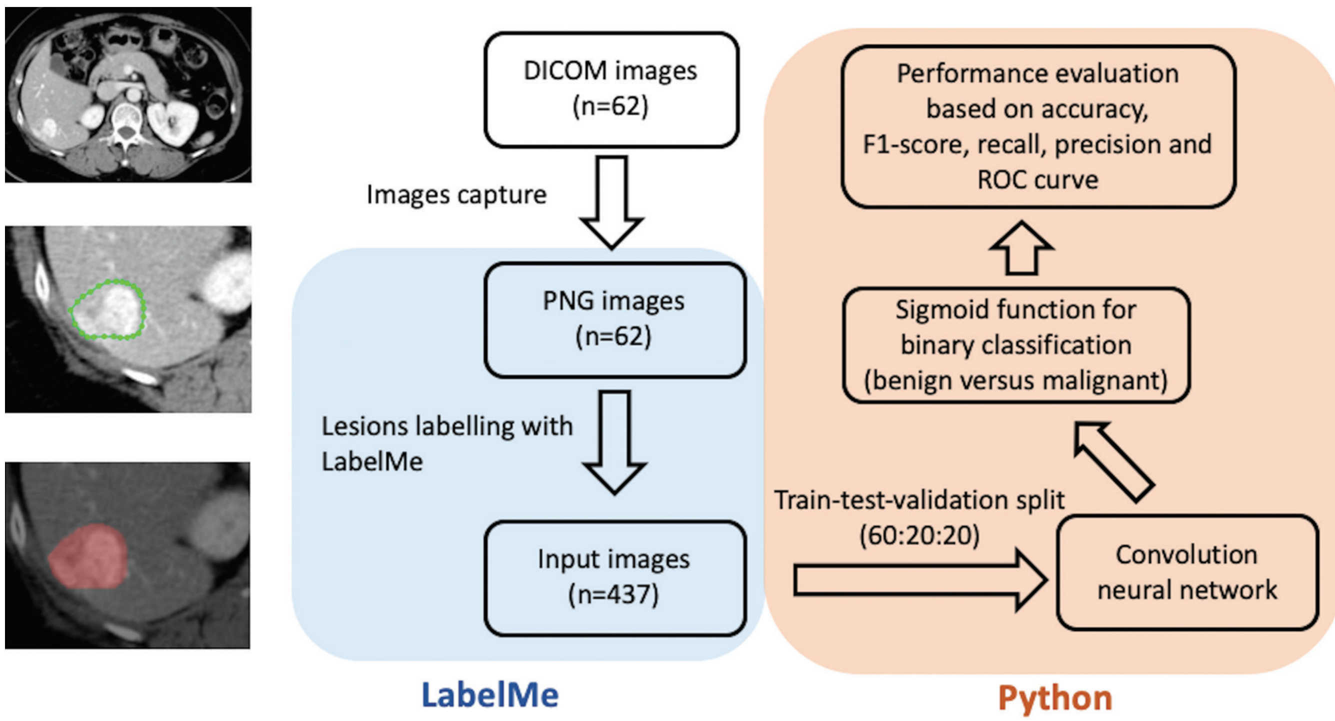

Figure 1: Flow chart of this study

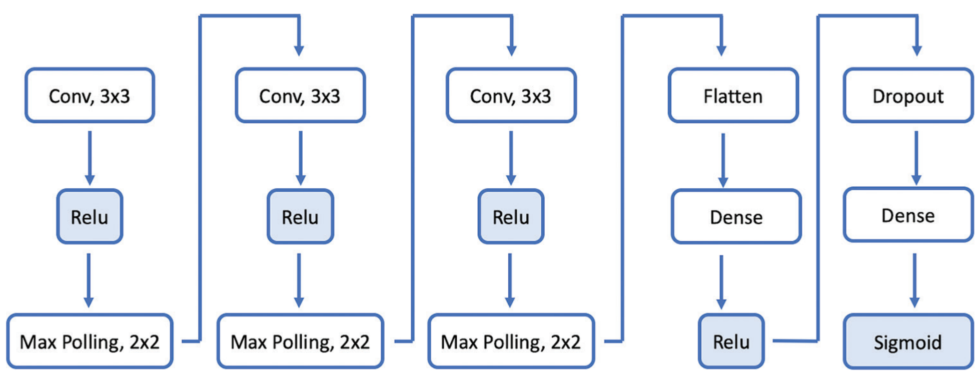

Figure 2: Architecture of convolutional neural network for binary classification of hepatic lesions

malignant lesions. The sigmoid function was often used in binary classification because of its differentiability, gradient properties, and convergence in training. During training, the weights were optimized through RMSprop optimization with a batch size of 64. The number of epochs was set to 50. Binary cross entropy was selected as loss function and was defined as:

$$L_{\mathrm{BCE}} = -\frac{1}{n}\sum_{i=1}^{n}(Y_i \times log\widehat{Y}_i + (1 - Y_i) \times log(1 - \widehat{Y}_i))$$

Evaluation of performance

The methods are evaluated quantitatively using accuracy, precision, recall, *F* score, and receiver operating characteristic (ROC) curves. These are computed as:

(1) $\text{Accuracy} = \dfrac{\text{TP} + \text{TN}}{\text{TP} + \text{FN} + \text{TN} + \text{FP}}$

(2) $\text{Precision} = \dfrac{\text{TP}}{\text{TP} + \text{FP}}$

(3) $\text{Recall} = \dfrac{\text{TP}}{\text{TP} + \text{FN}}$

(4) $F\text{-score} = \dfrac{2 \times \text{Precision} \times \text{Recall}}{\text{Precision} + \text{Recall}}$

RESULTS

There were 214 images of benign hepatic lesions and 223 images of malignant hepatic lesions enrolled in this study, including 84 hemangiomas, 131 hepatic cysts, 146 HCC, and

77 hepatic metastatic lesions. CNN model achieved the best results to classify benign and malignant hepatic lesions, with an average validation accuracy of 0.91 [Table 1]. For precision, recall, and F-score, the trained CNN model can achieve 0.89, 0.91, and 0.90 for benign lesions, respectively; for malignant lesions, it can achieve 0.92, 0.91, and 0.92, respectively.

Confusion matrix [Figure 3] demonstrated that 5 of 65 (7.69%) malignant hepatic lesions were predicted as benign in the CNN model; with 6 of 55 (10.9%) benign hepatic lesions predicted as malignant. The ROC curves of the CNN models showed area under the curve of 0.96 [Figure 4].

DISCUSSION

This single-center retrospective study aimed to use CNN to perform binary classification of benign and malignant hepatic lesions with portal venous phase CT images. Our results proved that CNN can classify hepatic lesions with acceptable accuracy, with a low false-negative rate for malignant hepatic lesions.

A CNN is a well-known and widely-used deep learning algorithm designed for processing structured grid data such as images. CNNs have shown its ability in computer vision tasks such as image classification, object detection, and image generation, and have been introduced into the field of liver CT imaging for both segmentation[13] and lesion classification.[10,11]

Table 1: Precision, recall, and F1-score of binary classification of benign and malignant hepatic lesions

	Benign hepatic lesions	Malignant hepatic lesions
Precision	0.89	0.92
Recall	0.91	0.91
F1-score	0.90	0.92

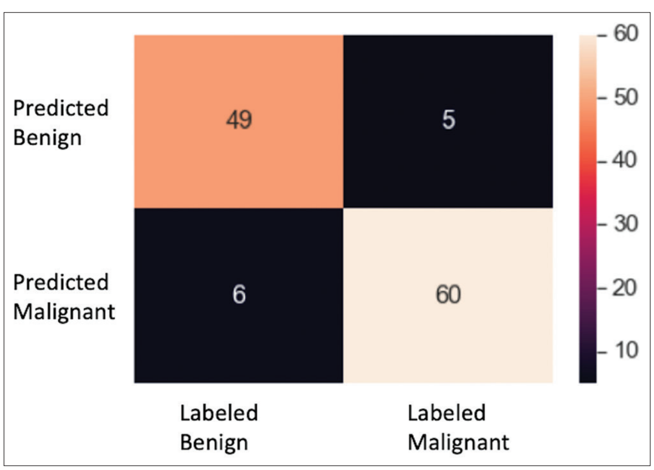

Figure 3: Confusion matrix of binary classification of benign and malignant hepatic lesions

U-net,[14] which is the most popular organ segmentation method in the past decade, is based on the architecture of CNN. Zhou *et al*.[10] used three phases of CT scan (unenhanced phase, arterial phase, and portal venous phase) to classify hepatic lesions with CNN, and reach an acceptable accuracy of 82.5%. Yasaka *et al*.[11] performed lesions classification with dynamic CT (which means that it contains an unenhanced phase, arterial phase, portal venous phase, and delayed phase) under the assistance of CNN, and it reached a median accuracy of 0.84.

The above-mentioned studies performed the classification of hepatic lesions with multiphasic CT images. For radiation dose, multiphasic abdominal–pelvis CT has a higher radiation dose (median value of 31 mSv) in comparison with routine abdominal–pelvis CT with contrast (including unenhanced phase and portal venous phase) (median value of 16 mSv);[15] higher radiation dose indicates higher associated lifetime attributable risk of cancer. Besides, multiphasic CT scan needs longer scanning time and higher health expenditure, causing economic pressure to the health-care system. This study focused on the binary classification of hepatic lesions with portal venous phase CT images. In clinical settings, the portal venous phase CT images play a fundamental role in the diagnosis of abdominal disease and contain more diagnostic information than other phases. This experimental design is more practical in comparison with multiphasic CT design as applying to a real-world medical environment. In this study, 7.69% of malignant hepatic lesions were predicted as benign, and 10.9% of benign hepatic lesions were predicted as malignant. That is, in the clinical setting, <10% of malignant hepatic lesions were misrecognized as benign; these false-negative values should be as low as possible in the real-world diagnosis.

There are some limitations of this study. First, this was a single-center study, and the relatively small dataset potentially

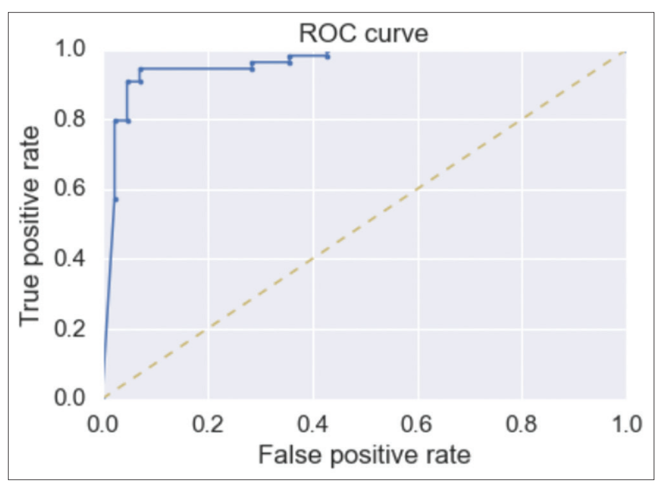

Figure 4: Receiver operating characteristic curve of binary classification of benign and malignant hepatic lesions

leading to a generalization (domain-shift) issue. Further investigation is necessary to enhance the robustness of this CNN model. Second, manual labeling was performed in this study, which may be a disadvantage in performing larger dataset experiments. Auto-segmentation should be selected in the further workup. Third, only binary classification was evaluated in this study. In clinical practice, classification for more precise diagnosis may be needed. Fourth, in this study, malignant hepatic lesions only enrolled HCC and liver metastases. Another nonrare malignant hepatic lesion, cholangiocarcinoma, was not included. Fifth, for liver metastases, the origin of malignancy may also lead to different imaging presentations, which is a potential bias for CNN to perform binary classification.

CONCLUSION

Binary classification of benign and malignant hepatic lesions with CNN can reach acceptable accuracy with portal venous phase CT images in a limited dataset, which could help inexperienced or primary physicians reach an initial diagnosis for undetermined hepatic lesions.

Data availability statement

The data that support the findings of this study are available from the corresponding author, W.C.Chang, upon reasonable request.

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Conflicts of interest

There are no conflicts of interest.

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