Identifying Periapillary Regions in MRI Images Using Deep Learning

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Identifying Periapillary Regions in MRI Images Using Deep Learning

Running title: Segmentation of Periapillary Regions Using Deep learning

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Abstract

Background: Development and validation of a deep learning method to automatically segment the peri-ampullary (PA) region in magnetic resonance imaging (MRI) images.

Methods: A group of patients with or without periampullary carcinoma (PAC) was included. The PA regions were manually annotated in MRI images by experts. Patients were randomly divided into one training set and one validation set. A deep learning method to automatically segment the PA region in MRI images was developed using the training set. The segmentation performance of the method was evaluated in the validation set.

Results: The deep learning algorithm achieved optimal accuracies in the segmentation of the PA regions in both T1 and T2 MRI images. The value of the intersection over union (IoU) was 0.67 and 0.68 for T1 and T2 images, respectively.

Conclusions: Deep learning algorithm is promising with accuracies of concordance with manual human assessment in segmentation of the PA region in MRI images. This automated non-invasive method helps clinicians to identify and locate the PA region using preoperative MRI scanning.

Keywords: Peri-ampullary cancer, MRI, Deep learning, Segmentation

Introduction

Periampullary carcinoma (PAC) usually occurs within 2cm of the main papilla of the duodenum, including four different types of malignant tumors, namely ampullary carcinoma, pancreatic head carcinoma, lower segment carcinoma of the bile duct, and duodenal carcinoma.¹⁻³ PAC is one of the most lethal malignant tumors in the gastrointestinal malignancies, accounting for 0.5-2.0% of the annual diagnosis of gastrointestinal

malignancies.⁴ The peri-ampulla (PA) region is deep and narrow in the abdomen. Meanwhile, due to the multiple kinds of lesions in PA, as well as the lack of special serum markers, it is particularly difficult to early diagnose tumors accurately, which lead to poor prognosis of PAC.^{5, 6} Currently, non-invasive diagnostic methods, including ultrasound scan, computed tomography (CT) imaging as well as magnetic resonance imaging (MRI), have been successfully applied to the detection and diagnosis of PAC.^{7, 8} So far, among all these modern imaging techniques, MRI is a preferable choice to detect PAC for its advantages of excellent soft-tissue contrast and less radiation exposures.^{6, 9} However, the accuracy and specificity of MRI are still unsatisfying in the diagnosis of PAC. One study has reported that the specificity of MRI was only 78.26%, while the accuracy was 89.89% in the diagnosis of PAC.⁶ Similarly, our previous study found that MRI had only 87% accuracy in detecting PAC.¹⁰ Besides, there is also the possibility that some benign diseases might be misdiagnosed as malignant diseases, such as chronic mass pancreatitis, the inflammatory stricture of the common bile duct, and common bile duct stone, et al. If the wrong surgeries were performed on these patients with benign diseases, it could be a disaster for them.¹¹ Therefore, it is necessary to further improve the diagnostic efficiency of MRI for the diagnosis of PAC.

Deep learning is an emerging sub-branch of artificial intelligence that has demonstrated transformative capabilities in many domains.¹² Technically, deep learning is a type of neural network with multiple neural layers that is capable of extracting abstract representations of input data like images, videos, time series, natural languages, and texts. Recently, there is a remarkable research advance of applying deep learning in healthcare and clinical medicine.¹³⁻

¹⁵ Deep learning has applications in the analysis of electronic health records, physiological data, and especially in the diagnosis of diseases using medical imaging.¹⁶ In the analysis of

medical images of MRI, CT, X-ray, microscopy, and other images, deep learning shows promising performance in tasks like classification, segmentation, detection, and registration.¹⁷

This brings both opportunities and challenges for clinicians, especially for radiologists.¹⁸

More recently, considerable literature has grown up in analyzing a variety of regions of interest (ROI) in the human body using deep learning. However, the PA region remains a largely under-explored ROI in medical image analysis based on advanced deep learning algorithms. Though the neural networks have been applied to classify ampullary tumors, the images were taken by endoscopic during operations rather than preoperative and non-invasive MRI or CT scanning.¹⁹ To our best knowledge, there is no reported work has been devoted to develop and evaluate deep learning methods to segment the PA region in MRI images.

Therefore, in this study, we presented a deep learning method to automatically segment and locate the PA region in MRI images. We retrospectively collected an MRI image dataset from PAC and normal peri-ampullary field patients. In a training-validation approach, we developed the deep learning method in the training set and validated the performance in the validation set.

Materials and Methods

The overall workflow of this study was illustrated in **Figure 1**. First, patients were enrolled, and the MRI images were obtained. Next, the PA regions were annotated in the raw MRI images by experts. Using the raw images and annotation information, the deep learning segmentation algorithms were trained and evaluated in training and validation datasets, respectively. Finally, the performance was summarized and reported.

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97 **Figure 1:** Overall flowchart of this study. First, MRI images were obtained from enrolled
 98 patients and manually annotated by experts to obtain the masks for later training and

validation. The dataset was randomly divided into two sets for algorithm training and validation, respectively. Five models were developed, and the UNet16 achieved the best performance.

Patients characteristics

This was a retrospective study approved by the Ethics Committee of the Affiliated Hospital of Southwest Medical University and written informed consent was obtained from all patients (No.KY2020157). A total of 504 patients who underwent abdominal MRI examinations were enrolled in this study. In these people, 88 persons were diagnosed as peri-ampullary carcinoma through pathology after surgery or endoscopy, and the other 416 persons show no peri-ampullary lesion determined by radiologist. All patients were underwent MRI examinations. Meanwhile, demographic (eg, age and gender) and clinical characteristics were recorded.

MRI techniques

After 3-8 hours of fasting, patients were asked to practice their breathing techniques. MRI was performed in all patients with a 3.0-T MR equipment (Philips Achieva, Holland, Netherlands) with a quasar dual gradient system and a 16.0-channel phased-array Torso coil in the supine position. Drinking water or conventional oral medicines were not restricted. The MR scan started with the localization scan, followed by a sensitivity-encoding (SENSE) reference scan. The scanning sequences were as follows: breath-hold axial dual fast field echo (dual FFE) and high spatial resolution isotropic volume exam (THRIVE) T1-weighted imaging (T1WI), respiratory triggered coronal turbo spin echo (TSE) T2-weighted imaging (T2WI), axial fat-suppressed TSE-T2WI, single-shot TSE echo-planar imaging (EPI) diffusion-weighted imaging (DWI), and MR cholangiopancreatography (MRCP). For the dynamic contrast enhancement (DCE)-MRI, axial-THRIVE-T1WI were used. 15mL of contrast agent Gd-DTPA was injected through the antecubital vein at a speed of 2mL/s. DCE-

MRI was performed in three phases, including arterial, portal, and delayed phase, and images were collected after 20s, 60s, and 180s, respectively¹⁰. In result, among the 504 patients, 485 patients had THRIVE-T1W images (n = 5,861), and 495 patients had T2 W images (n = 2,558).

MRI imaging analysis

Post-processing of MRI images was performed using the Extended MR Workspace R2.6.3.1 (Philips Healthcare) with the FuncTool package. All imaging examinations and measurements were performed on the workstation by two experienced radiologists who were blinded from the clinical and pathological findings, and evaluation was performed by the same observational items and criteria. Disagreements over the findings between the two radiologists were resolved by consensus. MRI showed typical PAC imaging manifestations: (1) the mass was nodular or invasive; (2) Tumour parenchyma on T1WI was equal or marginally lower signals; (3) Tumour parenchyma on T2WI was equally or slightly stronger signal; (4) DWI showed high signal intensity; (5) the mass was mild or moderate enhancement after contrast; and (6) when MRCP was performed, the bile duct suddenly terminated asymmetrically and expanded proportionally (double-duct signs may occur when the lesion obstructed the ducts¹⁰).

Pathological examination

The pathological data from all of the cases were analyzed by two pathologists with more than 15 years of diagnostic experience. The pathologists were blinded to the clinical and imaging findings.

Image annotation

First, all raw MRI images were annotated by two experienced radiologists using in-house software. In the annotation, one radiologist was required to manually draw the ROI outlines of the PA regions in the raw MRI images. The outline information was used to generate a

corresponding mask image in the same size to indicate the segmentation and of the ROI. An expert radiologist reviewed all manual annotations to ensure the quality of the annotations, which served as ground truths to develop and validate deep learning algorithms.

Among the 504 patients, 485 patients had T1 images ($n = 5,861$), and 495 patients had T2 images ($n = 2,558$) were processed separately. We treated the segmentations of T1 and T2 images as independent tasks. To avoid train-validation bias, we first randomly divided the patients into two cohorts, namely one training cohort (90%) and one validation cohort (10%). Their raw images and corresponding annotated mask images were also accordingly grouped into one training set and one validation set, respectively. In other words, the raw and mask images of the training cohort were used to train deep learning algorithms, and those images of the validation cohort were later used to validate the performance of deep learning algorithms.

Deep learning methods

In this study, we developed deep learning algorithms using multiple layers of convolutional neural network (CNN) to automatically segment the ROI of the PA region in MRI images. CNN is usually utilized to extract hierarchical patterns from images in a feedforward manner. CNN-based deep learning algorithms have achieved remarkable performance in many computer vision applications surpassing human experts.¹² In medical image analysis, UNet adopted a two-blocks structure utilizing multiple layers of CNN.²⁰ More specifically, the architecture consisted of two components, namely one encoder transformed the high dimensional input images into low dimensional abstract representations, and one following decoder projected the low dimensional abstract representations back to the high dimensional space by reversing the encoding. Finally, generated images were output with pixel-level label information indicating the ROI part. The detailed structure was illustrated in **Figure 2**. In order to systematically investigate the performance of the deep learning approach, in this

study, we also considered another four structure variations, namely ATTUNet using the attention gate approach in UNet,²¹ FCNRES50 using RESNet50 as the downsampling approach,²² UNet16 use VGG16 as the downsampling approach,²³ and SUNet using SeLu as the nonlinear activation function instead of ReLu.

Figure 2: Schematic diagram of the proposed deep learning algorithm with the UNet16 based on an Encoder-Decoder architecture. The encoder was a down-sampling stage, while the decoder was an up-sampling stage. Raw images and ground truth masks were input into the network to obtain the predicted segmentation.

In the deep learning algorithm training stage, the raw MRI images of the training cohort were input into the encoder one by one. The output masks generated by the decoder were compared against the corresponding ground truth to calculate the loss function, which indicated the deviations of predicted segmentation. By using the back-propagation technique of stochastic gradient descent optimization, the encoder-decoder structure was continuously optimized to minimize the loss. More technically, the weights between neural network layers were adjusted to improve the capability of segmentations. Once the training started, both the encoder and decoder were all trained together. In this manner, a satisfying deep learning neural network could hopefully be obtained after training with enough training samples.

Meanwhile, since the input and output were both images, this deep learning approach enjoyed significant advantages over the conventional image analysis methods by eliminating the exhausting feature engineering or troublesome manual interferences. After the training stage, the trained encoder-decoder structure was used in passive inferences to predict ROI in raw images. In inferences, the weights were kept unchanged. In the validation stage, the raw MRI images of the validation set were input into the neural network, and the corresponding mask images were obtained. We considered four different variations of the U-Net structure to seek the best performing deep learning structure. Deep learning algorithms for T1 and T2 MRI images were trained and validated separately using respective images.

All programs were implemented in Python programming language (version 3.7) with freely available open-source packages including Opencv-Python (version 4.1.0.25) for image and data processing, Scipy (version 1.2.1) and Numpy (version 1.16.2) for data management, Pytorch (version 1.1) for deep learning framework, Cuda (version 10.1) for graphics processing unit (GPU) support. The training and validation were conducted in a computer installed with an NVIDIA P40 deep learning GPU, 20GB main memory, and Intel(R) Xeon(R) 2.10GHz central processing unit (CPU). It is worth mentioning that the validation task could be done using a conventional personal computer within an acceptable time since the passive inference requires fewer computations.

Statistical evaluation of segmentation

The performance of the segmentation task for the ROI of the PA region in MRI images was quantitatively evaluated using intersection over union (IoU) and Dice similarity coefficient (DSC). For one PA region instance in an MRI image, the manually annotated ground truth ROI and the deep learning predicted ROI were compared at pixel-level to see how the two regions overlapped. In general, larger values of IoU and DSC indicated better segmentation accuracies. The average IoU and DSC were calculated based on predictions for all images in

the validation set. For simplicity, we used IoU as the main measurement, and the performance of five deep learning structures was ranked according to IoU. The predictions of T1 and T2 MRI images were conducted separately in the same manner.

Results

Patients characteristics

We identified 504 persons who had abdominal MRIs. Among them, 88 patients were diagnosed as PAC through pathology after surgery or endoscopy, and the other 416 persons showed no peri-ampullary lesion determined by radiologists.

MRI images

In preparing the training and validation datasets, we intended to divide the initial dataset based on patients to ensure that images from the same patient would only appear simultaneously in the training or validation sets. Furthermore, since the segmentation for T1 and T2 MRI images were conducted separately, we prepared the training image set and validation image set for T1 and T2 also separately. In result, for T1 images ($n = 5,861$), the training set included 5,321 from 436 patients, the validation set included 540 images from 49 patients. For T2 images ($n = 2,588$), the training set included 2,319 images from 446 patients, and the validation set included 239 images from 49 patients.

Segmentation performance

For the five segmentation deep learning structures, we followed the same training approach in separated training and validation of T1 and T2 images, namely each image formed a batch (batch size = 1), and four rounds were repeated (epoch = 4) to ensure the convergence of the loss. The final segmentation performance of all five structures was presented in **Table 1** for T1 images and **Table 2** for T2 images, respectively. We found that UNet16 outperformed all the rest structures with the best performance for both of T1 (IoU = 0.67, DSC = 0.78) and T2

(IoU = 0.68, DSC = 0.80), respectively. **Figure 3** demonstrated the segmentation samples obtained by UNet16 for T1 and T2 images.

Table 1 Segmentation performance of deep learning structures in T1 images ranked by mean IoU. UNet16 achieved the best performance.

Model	IoU		DSC	
	Mean	Std. Dev.	Mean	Std. Dev.
UNet16	0.67	0.21	0.78	0.21
FCNRES50	0.52	0.33	0.60	0.36
UNet	0.47	0.33	0.56	0.36
ATTUnet	0.47	0.33	0.56	0.37
SUnet	0.31	0.30	0.39	0.35

Table 2 Segmentation performance of deep learning structures in T2 images ranked by mean IoU. UNet16 achieved the best performance.

Model	IoU		DSC	
	Mean	Std. Dev.	Mean	Std. Dev.
UNet16	0.68	0.15	0.80	0.15
FCNRES50	0.58	0.23	0.70	0.25
UNet	0.52	0.27	0.63	0.31
ATTUnet	0.46	0.26	0.58	0.29
SUnet	0.41	0.25	0.53	0.29

Figure 3: Examples of PA regions annotated by experts (left) and the corresponding segmentation results obtained by UNet16 deep learning structure (right). A, The top panel was an example of T1 MRI image; B, The bottom panel was an example of T2 MRI image.

Discussion

PAC occurs in 5% of gastrointestinal tumors, and pancreatic cancer is the most common, followed by distal cholangiocarcinoma.^{2, 24} Pancreatoduodenectomy (PD) was the standard treatment for patients with PAC.²⁵ However, complications such as pancreatic fistula, biliary fistula, infection, and hemorrhage often occur after PD surgery. A previous study has shown

that the incidence of postoperative complications of PD may be as high as 30-65%.²⁶ For patients with benign lesions, unnecessary PD surgery could lead to the occurrence of these surgical complications in patients, or even death in some patients. Meanwhile, if malignant lesions are misdiagnosed as benign lesions, it will undoubtedly delay the treatment of patients, resulting in poor prognosis. Due to the anatomical complexity of the perampullary region and less of particular serum markers, the early-accurate diagnose of PAC still remains challenging. In recent years, magnetic MRI with MR cholangiopancreatography (MRCP) has been reported to be an optimal choice for allowing assessment of perampullary lesions.²⁷ However, due to the difficulties of MRI in detecting masses of the perampullary area in primary stages or make a definitive diagnosis, the accuracy and specificity of MRI are still unsatisfying in the diagnosis of PAC. Recently, with the significant development in deep learning and increasing medical needs, artificial intelligence technology has significant advantages in improving the diagnosis of diseases. Therefore, we propose to combine AI technology with MRI to diagnose PAC. However, considering the particularity of the PA region, we firstly proposed and developed a deep learning method to automatically segment the PA region in MRI images, which was supposed to further facilitate the PAC assisted diagnosis.

In this work, we developed deep learning structures to automatically segment the PA region using MRI T1 and T2 images. To our best knowledge, there is no existing work applied deep learning approaches for the segmentation of the PA regions in MRI images. To systematically evaluate the performance of various deep learning structures, we implemented five algorithms that appeared in deep learning literature, including UNet,²⁰ ATTUNet,²¹ FCNRES50,²⁸ UNet16,²⁹ and SUNet. UNet was the most used deep learning structure in medical image analysis using the encoder and decoder components based on CNN.²⁰ The rest

variations improve the UNet structures with attention or replace nonlinear activation functions. This study considered these structures and compared their performance in the same datasets.

In total, 504 patients were included in this study, and 5,861 T1 images and 5,321 T2 images were collected. All images were manually annotated by experts to delineate the PA regions in the MRI images. By dividing patients into training and validation cohorts, their images were split into a training set for algorithms training and a validation set for final performance evaluation. In result, UNet16 achieved the best performance among the five structures with the highest IoU of 0.67 and DSC of 0.78 for T1 images, and IoU of 0.68 and DSC of 0.80 for T2 images. The results showed that UNet16 was able to accurately identify the PA region in MRI images.

However, there are still several limitations in this study. First, we only used AI to do preliminary localization of MRI images of peri-ampullary cancer and did not make a diagnosis. In the future, we would collect more data and extend the present deep learning framework to classify and diagnose PAC. Second, this is a retrospective study from a single hospital, which may inevitably lead to selective bias for the patients. The results need to be validated by prospective and external cohorts. Third, the applied AI technologies in this study are still in rapid evolution with more emerging advanced deep learning algorithms. In the future, it's necessary to evaluate new deep learning algorithms in PAC image analysis to achieve better performance.

In conclusion, we established an MRI image dataset, developed an MRI image data annotation system, established an automatic deep learning PAC image segmentation model, and realized the location of the tumor area. This study has important clinical value in improving the accuracy and efficiency of PAC diagnosis and enhancing the clinical treatment effect of PAC.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and Ethical Guidelines for Clinical Research. This was a retrospective study approved by the Ethics Committee of the Affiliated Hospital of Southwest Medical University and written informed consent was obtained from all patients (No.KY2020157).

Consent for publication

All authors read and approved the final manuscript.

Availability of data and materials

The datasets used and analysed during the current study available from the corresponding author on reasonable request.

Competing interests

The authors deny any conflicts of interest.

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Authors' contributions

Yong Tang, Xinpei Chen, Weijia Wang, Jiali Wu, Yingjun Zheng, Qingxi Guo, Jian Shu, and Song Su conceived and designed the study, and were responsible for the final decision to submit for publication. All authors were involved in the development, review, and approval of the manuscript. All authors read and approved the final manuscript.

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Figures

Figure 1

Overall flowchart of this study. First, MRI images were obtained from enrolled patients and manually annotated by experts to obtain the masks for later training and validation. The dataset was randomly

divided into two sets for algorithm training and validation, respectively. Five models were developed, and the UNet16 achieved the best performance.

Figure 2

Schematic diagram of the proposed deep learning algorithm with the UNet16 based on an Encoder-Decoder architecture. The encoder was a down-sampling stage, while the decoder was an up-sampling stage. Raw images and ground truth masks were input into the network to obtain the predicted segmentation.

Figure 3

Examples of PA regions annotated by experts (left) and the corresponding segmentation results obtained by UNet16 deep learning structure (right). A, The top panel was an example of T1 MRI image; B, The bottom panel was an example of T2 MRI image.