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Deep Learning-Based Histological Scoring of Cerulein-Induced Acute Pancreatitis Rat Model

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***Abstract*—In an experimental rat model of acute cerulein-induced pancreatitis, we aimed to investigate the ability of the deep neural network-based program to distinguish damaged cell structures in histological preparations derived from rat pancreatic tissues. After the pancreatic tissues of all rats underwent the paraffin procedure, 3-4 µm thick sections were taken from the paraffin blocks, stained with hematoxylin-eosin dye, evaluated with a light microscope and photographed using a light microscope. 89 mixed-size microscopic images are resized at 224*224 diameter. The datasets were divided into train, validation and test groups. The algorithm used in this study was based on the NAS-Net-Mobile and ResNet-101 models from MATLAB Transfer Learning. By increasing the number of samples in the method we use in histology, both the evaluation performance and time consumption are reduced with the AI we use. The accuracy rate we obtained with NAS-Net mobile was determined to be higher than ResNet-101.**

Keywords—acute pancreatitis, artificial intelligence, deep learning

I. INTRODUCTION (*HEADING 1*)

Acute-pancreatitis (A-P) is a local and systemic inflammation that can cause pancreatic oedema, necrosis, organ failure or even death. A-P, which occurs in different severities, is a serious disease that causes acinar cell damage [1]. Acinar cell damage occurs due to the early release of proteolytic enzymes, reactive oxygen species (ROS) and inflammatory mediators in the A-P process, which occurs at different intensities (2). Oxidative stress and inflammation play an important role in pancreatic damage seen in A-P process [2-4].

Although any specific treatment is still not available for the A-P, the symptomatic treatment approaches are used. Additionally, determining the underlying causes of A-P and implementing effective treatment prevents the occurrence of acute recurrent pancreatitis defined as A-P attacks. Therefore, new experimental research is needed in this area.

The results obtained from the animal models are necessary and very important step in preclinical researches on the proposal of new ingredients and the research of new treatments. The cerulein-induced rat model is a widely used model of A-P [5, 6] and in the case of acute pancreatitis; vascular congestion, acinar dilation and atrophy, cellular vacuolization, and pancreatic inflammation are observed. In this study, acute oedematous pancreatitis is induced by the administration of cerulein, and the cerulein group is compared to the control group.

Histological examination of pancreatic tissue is a common method used in experimental studies [6]. It provides the detection of tissue damage caused by pancreatitis. However, it also brings some limitations. Firstly, due to a large number of samples in the microscopic examination, the length of the observation time for each slide and some limitations in personal observation, the sensitivity and duration of the evaluation can be affected. In addition, since the preparation and interpretation of these preparations take a long time, low damage detection and misinterpretations may occur during the long evaluation process. It is recommended to use Artificial Intelligence (AI) to solve these difficulties and limitations. Deep learning, enables the system to learn by creating a data model by taking data connections between all artificial neurons. Deep neural networks using feed-forward neuronal networks trained using the backpropagation algorithm are equipped with fully interconnected layers. Deep learning neural network is used by

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scientists to classify and analyse medical images and diagnosis of diseases.

Convolutional neural networks (CNNs), which have recently been a form of deep learning and assumed that the best CNNs in the object recognition task exceed human performance, are used in a wide range of biomedical applications and medical image processing tasks. It is clear that over the years, the number of histopathological/pathological image analyses will increase with deep learning styles.

The aim of this study was to investigate the ability of the Deep neural network-based program to distinguish damaged cell structures in the histological preparations obtained from pancreatic tissues in an experimental acute cerulein-induced pancreatitis rat model.

II. MATERIALS AND METHODS

A. Animals and conditions

For the current study, pancreatic tissue sections of previous rat studies run were used and reanalysed. Studies included 8 to 12 weeks of age, weighing 200-250 g and a total of 100 Wistar albino rats in both sexes. The whole rats used in the study were purchased from the Experimental Animals Application and Research Centre, Breeding Unit (Marmara University, Istanbul-Turkey). All rats were housed in plexiglass cages for a 12h/12h light/dark period. All rats were fed *ad libitum* without food and water restrictions.

B. Dataset

The pancreas tissues of all rats were immediately fixed with 10% formaldehyde solution for the histological evaluation. The collected pancreas tissue samples were undergoing routine histological paraffin procedure. 3-4 μm-thick sections were cut by rotary microtome from paraffin blocks including pancreas tissues and the sections were stained with hematoxylin-eosin dye to evaluate using light microscope (Olympus BX-51). The digital camera attached light microscopes (Olympus DP72, Tokyo, Japan) were used in bright field illumination using a 40x objective and photographed.

C. Image evaluation

Each slide of the pancreas tissues was evaluated morphologically, and semi-quantitative histological scoring was done using the Warzecha et al technique (2008) [7].

D. Classification model

89 mixed-sized microscopic images were resized 224*224 diameters. The datasets were divided into the train, validation, and test groups.

1. The Training Dataset contains 44 images.
2. The Validation Dataset contains 22 images.
3. The Testing Dataset contains 23 images.

Image augmentation is used to increase the number of images in the dataset. Images are rotated as well as vertically and horizontally flipped.

E. The architectures of a deep convolutional neural network (CNN)

ResNet-101:

Res-Net, which stands for Residual Networks, is the structure we used for our classification challenge and it contains an essential aspect of computer vision issues. ResNet network makes use of residual connections, via which gradients can pass directly, to prevent gradients from being zero following chain rule applications [8].

ResNet-101 has 104 convolutional layers in total, which are divided into 33 layers blocks, 29 of which directly use the output of the previous block, which are known as residual connections above. These residuals are then used as the first operand of the summation operator, which is used at the end of each block to obtain the input of subsequent blocks. The output from the preceding block is used in the remaining 4 blocks' convolution layer, which has a filter size of 1x1 and a stride of 1, then a batch normalization layer, which performs a normalization operation, with the resulting output being sent to the summation operator at that block's output [9].

NAS-Net-Mobile

NAS-Net is a scalable convolutional neural network (CNN) architecture that was built through neural architecture search and is made up of fundamental building elements (cells) that are reinforced and learning-optimized. Only a few operations—many separable convolutions and pooling—make up a cell, which is performed multiple times in accordance with the network's required capacity. There are 12 cells in the mobile version (NAS-Net -Mobile), 5.3 million parameters, and 564 million multiply-accumulates (MACs) [10]. All the block diagrams of methods are, shown as Fig 1.

F. Implementation

The algorithm used in this study was based on the NAS-Net Mobile and ResNet-101 models from MATLAB Transfer Learning. Computer tools from the Near East University Faculty of Engineering Innovation Laboratory were used to implement the training procedure. The NVIDIA® GeForce® RTX 2080 Ti GPU was used for all training and testing. The sgdm optimizer was used to train the network. There were 20 batches in total. The learning rate was set to 0.009. all the networks were trained for up to 30 epochs.

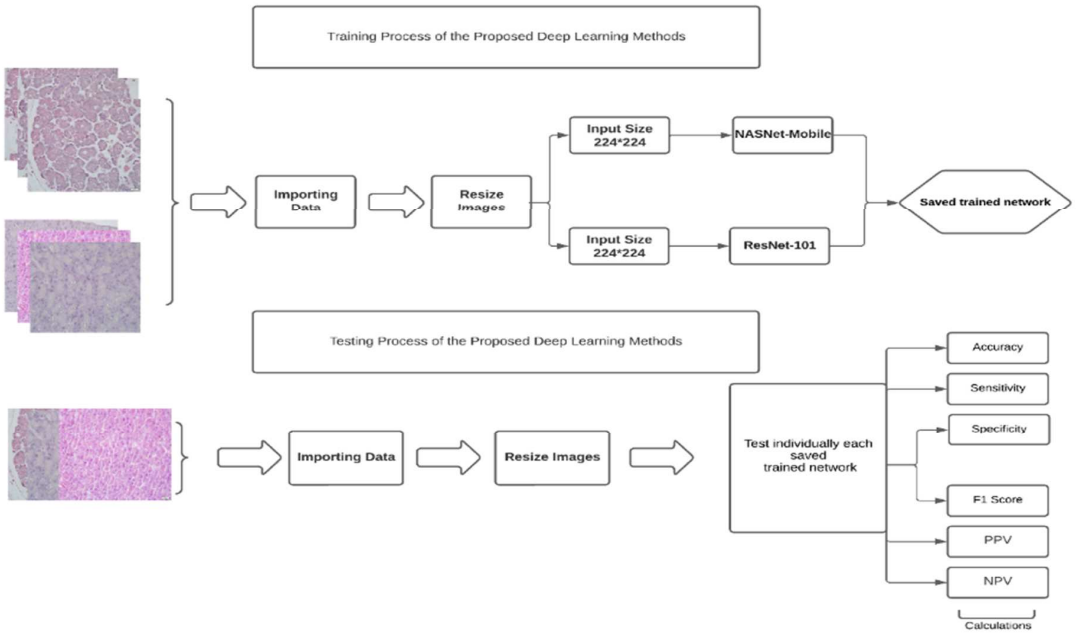

Fig. 1: Training and Testing Phase.

III. Result

A. Evolution Formulas

The effectiveness of the two models was evaluated. The following formulas are utilized in the procedure:

$$\text{Accuracy}=[TP+TN/TP+FP+TN+FN] \quad (1)$$

$$\text{Sensitivity}=[TP/TP+FN] \quad (2)$$

$$\text{Specificity}=[TN/TN+FP] \quad (3)$$

$$\text{F1Score}=[2TP/2TP+FP+FN] \quad (4)$$

$$\text{PPV}=[TP/TP+FP] \quad (5)$$

$$\text{NPV}=[TN/TN+FN] \quad (6)$$

Where the TP stands for true positive results, TN stands for true negative, FP is the false positive, and FN is the false negative.

B. Experimental Results

Model	Accuracy	Sensitivity	Specificity	F1 Score	PPV	NPV
NASNET-Mobile	0.95	1	0.92	0.95	0.90	1
ResNet-101	0.82	0.9	0.76	0.81	0.75	0.90

IV. Conculation

By increasing the number of samples in the method we use in histology, both the evaluation performance and time consumption are reduced with the AI we use. The accuracy rate we obtained with NAS-Net mobile was determined to be higher than Res-Net.

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