AN IMPROVED DIAGNOSTIC ALGORITHM BASED ON DEEP LEARNING FOR ISCHEMIC STROKE DETECTION IN POSTERIOR FOSSA

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For my beloved mother and father,

Sisters,

Best friend,

Friends,

Thank you for all of your support along the way.

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ABSTRACT

Ischemic stroke is triggered by an obstruction in the blood vessel of the brain, preventing the blood to flow to the brain tissues region. Solving this is extremely beneficial as Non-enhanced Computed Tomography (NECT) has significant shortcomings for posterior fossa (PF): (i) deficient sensitivity (ii) subtle finding and (iii) radiation exposure. Consequently, PF ischemic stroke lesions are missed at the early stage which increasing the mortality rates. Nowadays, the development of Computer-Aided Diagnosis (CAD) is increasingly becoming an important area in stroke detection. Despite the rapid development of CAD in stroke diagnosis, no studies have been found on stroke detection in PF. Until today, manual delineation of ischemic stroke in PF on NECT demands dealing with a large amount of data, which leads to late prognosis. As the amount of image data generated by NECT is massive, Deep Learning (DL) solutions are among the effective ways to deal with complex and large amount of cross-sectional data. Therefore, a new diagnostic algorithm based on DL is proposed for ischemic stroke detection in PF. The algorithm framework consists of hybrid of improved Xception model and YOLO V2 detector to classify the PF slices with ischemic and localise the infarction in classified slices, respectively. Following that, a CAD system is established by integrating the proposed algorithmic framework. The performance and effectiveness of the proposed algorithmic are evaluated by the comparison with the gold standard provided by the radiologists. The proposed algorithmic framework has shown to be less prone to overfitting and simultaneously improves the detection performance than the original DL model. The results demonstrate that the performance measure of 90.77% has been recorded for detection rate with average processing time of 1.02 to 1.04 seconds per image. The developed algorithm is reported to be reliable to assist the radiologist in ischemic PF diagnosis which is important for future healthcare needs.

ABSTRAK

Strok iskemik berlaku disebabkan oleh saluran darah pada otak yang tersumbat, yang menghalang pengaliran darah ke kawasan tisu otak. Penyelesaian kepada permasalahan ini sangat bermanfaat memandangkan Tomografi Berkomputer Sekata (NECT) mempunyai kelemahan yang ketara pada bahagian fosa posterior (PF) iaitu: (i) kekurangan sensitiviti (ii) penemuan yang tidak jelas dan (iii) pendedahan radiasi. Sebilangan besar strok iskemik di bahagian PF tidak dapat dikesan pada peringkat awal dan membawa kepada peningkatan kadar kematian. Kini, pembangunan sistem diagnosis yang berbantukan komputer (CAD) adalah penting dalam pengesanan strok. Namun, tiada kajian dijumpai mengenai pengesanan strok di bahagian PF. Sehingga hari ini, pengesanan strok iskemik pada bahagian PF menggunakan kaedah NECT dan ini memerlukan pengendalian jumlah data yang besar, dan mengakibatkan kelewatan prognosis. Penyelesaian Pembelajaran Mendalam (DL) merupakan antara cara yang berkesan untuk mengendalikan data keratan lintang dalam jumlah yang besar. Oleh itu, satu algoritma diagnostik baru berdasarkan DL dicadangkan untuk pengesanan strok iskemik pada bahagian PF. Rangka algoritma terdiri daripada gabungan model Xception dan pengesan YOLO V2 yang ditambah baik, berperanan untuk mengklasifikasikan dan menyetempatkan iskemik pada kepingan PF. Satu sistem CAD juga telah dibangunkan dengan mengintegrasikan algoritma seperti yang dicadangkan. Penilaian prestasi dan keberkesanan algoritma telah dijalankan dengan membuat perbandingan antara algoritma tersebut dengan piawaian emas yang ditentukan oleh ahli radiologi. Rangka algoritma ini telah menunjukkan pengurangan kecenderungan terhadap *overfitting* dan meningkatkan prestasi pengesanan berbanding model DL yang asli. Hasil kajian menunjukkan bahawa ukuran prestasi mencapai 90.77% untuk kadar pengesanan dengan purata masa pemprosesan 1.02 hingga 1.04 saat bagi setiap imej. Keandalan algoritma yang dibangunkan ini dapat membantu ahli radiologi melakukan diagnosis iskemik pada bahagian PF, dan boleh mengisi keperluan bidang penjagaan kesihatan pada masa akan datang.

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LIST OF SYMBOLS AND ABBREVIATIONS

2D	-	Two-Dimensional
ADAM	-	Adaptive Moment Estimation
AI	-	Artificial Intelligence
ANN	-	Artificial Neural Network
AUC	-	Area Under the Curve
BP	-	Back Propagation
CAD	-	Computer-Aided Diagnosis
CNN	-	Convolutional Neural Network
CTA	-	CT Angiography
CTP	-	CT Perfusion
DICOM	-	Digital Imaging and Communications in Medicine
DL	-	Deep Learning
FC	-	Fully Connected
FN	-	False Negative
FP	-	False Positive
FPR	-	False Negative Rate
GUI	-	Graphical User Interface
GPU	-	Graphic Processing Unit
HIS	-	Hospital Information System
HU	-	Hounsfield Unit
ILSVRC	-	ImageNet Large Scale Visual Recognition Challenge
IoU	-	Intersections over Union
ML	-	Machine Learning
MRI	-	Magnetic Resonance Imaging
NECT	-	Non-enhanced Computed Tomography
N_h	-	Hidden Neuron

NIHSS	-	National Institutes of Health Stroke Scale
PAC	-	Picture Archiving and Communication
PF	-	Posterior Fossa
R-CNN	-	Region-based CNN
ReLU	-	Rectified Linear Unit
RIS	-	Radiology Information System
RMSP	-	Root Mean Square Propagation
ROI	-	Region of Interest
SGD	-	Stochastic Gradient Descent
SSD	-	Single Shot Multidetector
SUS	-	System Usability Scale
SVM	-	Support Vector Machine
TN	-	True Negative
TP	-	True Positive
TPR	-	True Positive Rate
W_c	-	Window Centre
W_w	-	Window Width
YOLO	-	You Only Look Once

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CHAPTER 1

INTRODUCTION

This chapter provides an overview of research background while emphasizing current issues on ischemic stroke diagnosis in posterior fossa (PF), described in Sections 1.1 and 1.2. Subsequently, the objectives along with the scopes of research are presented in Sections 1.3 and 1.4, respectively. Research contributions and thesis outline are then briefly explained in Sections 1.5 and 1.6, respectively.

1.1 Project Overview

The major societal challenge in current global healthcare is dealing with rapid progression of ischemic stroke cases. According to Johnson *et al*. (2019), there were 5,528,232 deaths due to stroke in 2016 globally. During that year, the death toll in Malaysia was 14,302 as shown in Figure 1.1. Although the number of deaths is lower than other countries, the occurrence of people diagnosed with ischemic stroke in Malaysia gradually increasing at 29.5% annually (Aziz *et al*., 2015). Ischemic stroke is an injury where the arterial occlusion occurs within the brain due to the acute reduction in the blood supply. There are several well-known factors contributing to ischemic stroke such as hypertension, atrial fibrillation, prior history of stroke, smoking, diabetes, excessive alcohol intake and others (Boo *et al*., 2016).

Figure 1.1: Deaths for stroke in 2016 by location (Johnson *et al*., 2019)

In fact, for every minute of delayed treatment, this cerebrovascular disease continuously damages approximately 1.8 million neurons of the brain (Urdaneta & Bhalla, 2019). Previous studies suggests that it is very important for the radiologist to perform stroke imaging procedure in a rapid and efficient way (Cho *et al*., 2019; Kamal *et al*., 2018). The delay in early diagnosis and treatment would result in drastic spread of the ischemic area. Clinically, early diagnosis of ischemic stroke is imperative; however, currently it necessitates the application of expensive Magnetic Resonance Imaging (MRI) which available only at specialised centres or in private practice. Besides the compulsory clinical examination routine of the symptomatic, Non-enhanced Computed Tomography (NECT) becomes the available option for first line of stroke imaging. In general, NECT operates in fast acquisition, cost-efficient, and is widely available relative to MRI (Urdaneta & Bhalla, 2019).

Despite these advantages, it is well known that NECT is deficiently sensitive when attempting to detect ischemic in PF region (Kniep *et al*., 2020). This can be described by several facts: first, the loss of gray-white matter differentiation in PF region is visible which causes the resemblance of normal tissues; second, the beam hardening artifacts produced by thick bone and inadequate contrast resolution limits the performance of NECT (Austein *et al*., 2019; Wolff *et al*., 2020). The magnitude and complexity of diagnosis tasks require a great deal of skills and experience from the radiologist. Thus, an early ischemic diagnosis can be strenuous in the clinical practice.

Computer-Aided Diagnosis (CAD) has been widely developed in medical image analysis to provide support for the radiologist in the decision-making process (Dourado *et al*., 2019; Kanchana & Menaka, 2015; Tang *et al*., 2011; Tyan *et al*., 2014). Figure 1.2 illustrates the CAD workflow in supporting the standard review of medical diagnosis primarily in radiology. Hospital Information System (HIS) or Radiology Information System (RIS) has become the integral part of NECT and MRI system to provide patient health information. Radiologists can feasibly combine patient reports with images taken along with historical information from HIS or RIS in order to obtain a baseline. The image data retrieved during scanning procedure is transferred to the CAD system to facilitate the standard review process in the workstation.

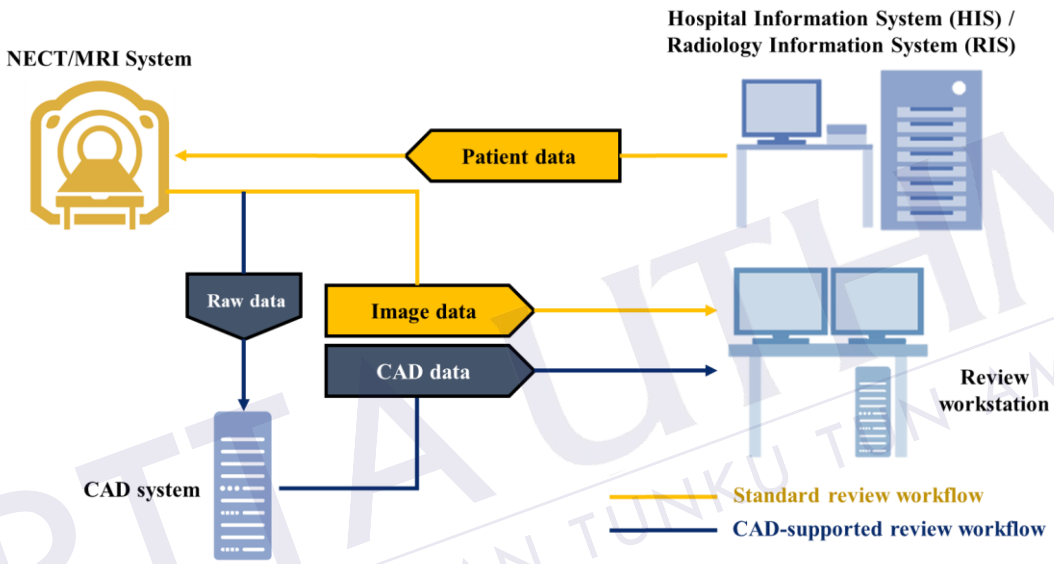

Figure 1.2: Standard and CAD-supported review workflow (Siemens Healthineers, 2018)

There are various techniques applied in the CAD to classify normal and ischemic NECT slices using traditional Machine Learning (ML) based method. Typically, these CAD systems begin with pre-processing, followed by hand-crafted feature extraction and classification steps to segregate normal and abnormal slices (Kanchana & Menaka, 2015, 2017; Kniep *et al*., 2020; Tang *et al*., 2011). Texture and intensity features are the examples of features which have been extracted to be fed into Support Vector Machine (SVM), Artificial Neural Network (ANN) and K-Nearest Neighbour (KNN) as the input (Aggarwal & Agrawal, 2012; Kanchana & Menaka, 2015, 2017; Kniep *et al*., 2020; Tang *et al*., 2011).

Deep Learning (DL) has made a breakthrough in medical image classification owing to its superior performance in solving a wide range of radiology cases (McBee *et al*., 2018; Suzuki, 2017). Contrary to the conventional ML methods, DL is capable to directly learn the features of an image without a hand-crafted feature extraction step. The emergence of DL in medical image classification with diseases such as Alzheimer, brain tumour ischemic infarction and dementia are tremendously increasing with high performance (Talo *et al*., 2019). Moreover, studies and research has been recently conducted to investigate the possibility of ischemic image classification with acute condition based on the DL method (Chin *et al*., 2018; Dourado *et al*., 2019; Pereira *et al*., 2018).

For all the aforementioned reasons, an automated diagnostic algorithm-based DL of ischemic stroke in PF slice of NECT is developed as a supportive platform to assist radiologists in their decisions. Besides that, the diagnosis from NECT image can be significantly improved by implementing CAD in conjunction with clinical evaluations. This proposed work can assist radiologists in clinical decision-making with numerous amounts of NECT images. In comparison with other works, this study offers the advantage of classifying as well as localising the ischemic in PF. The overall performance is evaluated using quantitative and qualitative approaches to assess the practicality and reliability of the developed system.

1.2 Problem Statement

According to Pereira *et al*. (2018), Asians contribute to the highest mortality rates of stroke than Westerners. Stroke remains as the third leading cause of mortality in Malaysia with 74.8% of patients experiencing their first episode of ischemic (Kooi *et al*., 2016). Ischemic stroke is due to the presence of blood clot or thrombus in the blood vessel. This type of stroke is relatively challenging to be identified specifically in PF region. Until now, NECT is the solely available option for early assessment of ischemic (Austein *et al*., 2019; Kniep *et al*., 2020; Vilela & Rowley, 2017; Wolff *et al*., 2020). Due to its prevalent, rapid acquisition and cost-efficient nature, NECT is the first option in almost every medical centre.

The ambiguous nature of decision-making process highly depends on the experience of radiologists and can be adversely affected by the high intra- and inter-observer variability (Kamal *et al*., 2018). Manual diagnosis of NECT images is monotonous and highly prone to errors (Ker *et al*., 2017). False positive cases usually occur because of the behavioural nature of acute ischemic in loss of gray-white matter differentiation which is nearly similar to normal tissues. This incident is depicted in

Figure 1.3. Another critical issue related to NECT in acute ischemic is poor sensitivity (Zürcher *et al*., 2019). The signs of early ischemic changes in PF are often subtle as NECT has low sensitivity of 41.8% in the first 24 hours of ischemic lesion inspection (Hwang *et al*., 2012). Urdaneta & Bhalla (2019) have also reported that ischemic PF is generally misdiagnosed for patients with dizziness symptoms. This is caused by the existence of beam hardening artifacts due to the amount of bones in PF region and time delay for strokes to emerge on the neuroimaging in the white matter relative to the gray matter (Hixson *et al*., 2016).

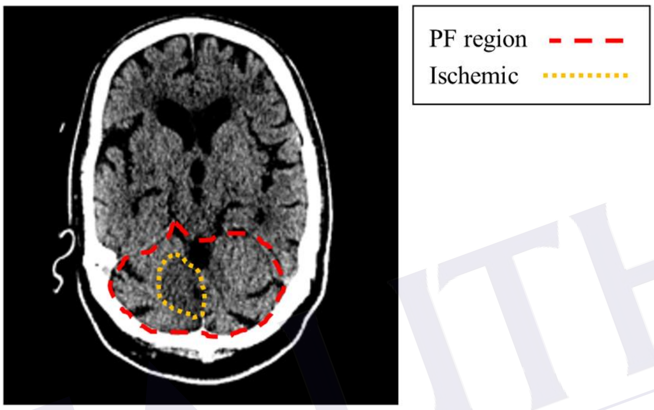

Figure 1.3: Ischemic stroke detection in PF region

An early diagnosis of ischemic in PF is extremely important to prevent brainstem infarction which can impact the prolonged state of the patient (Kniep *et al*., 2020). This incident needs to be promptly recognised in order to initiate adequate therapy and alleviate rate of mortality. In addition, the deficiency of well-trained and experienced radiologists in medical centres lead the decision-making phase to be performed by non-expert medical professionals (Kamal *et al*., 2018). Thus, this explains the need for effectiveness and timely implementation of a robust second opinion system that can assist these non-experts in interpreting and diagnosing diseases with higher confidence level.

Based on these circumstances, a diagnostic algorithm-based DL can be introduced to detect the ischemic PF stroke. This approach can bring about improvements in the ischemic diagnosis of PF region and subsequently reducing the mortality rates among patients. This proposed work may benefit the radiologist with efficient and accurate clinical assessment of ischemic PF stroke. Practically, their competence in analysing complex cases of this incidence can be enhanced through the perspectives of a wide range of DL technology.

1.3 Aim and Objectives

This research aims to develop a diagnostic algorithm which can classify and detect ischemic stroke in PF slice for early sign of stroke clinical assessment. To achieve the aim, the following objectives have been outlined:

1. To develop a new automated classification method of ischemic in PF slices.
2. To construct a hybrid DL architecture that supports rapid and efficient detection of ischemic in PF slices.
3. To evaluate the performance of the developed algorithm via a series of experimental programme (quantitative and qualitative analysis).

1.4 Scopes and Limitations

The restrictions and limitations in terms of the dataset, method and working platform, during this research are:

1. This study focuses on the development of diagnostic algorithm for ischemic stroke classification and detection in PF using Convolutional Neural Network (CNN) approaches because of its high accuracy in medical image processing.
2. The medical institution collaborator is UKM Medical Centre. All the ethical standards are conducted by the radiologist. Approval is obtained for this retrospective study.
3. The head NECT slices used in this study is scanned by using Toshiba Aquilion ONE scanner following standardised parameters specified by the radiologist. Only dataset from similar machine is included as accurate analysis can be achieved using similar scanning parameters.
4. The experimental studies are conducted on ischemic stroke infarction in PF slices under brain NECT imaging with a restricted number of patients. Due to a vast variation in shapes, sizes and locations of PF, it is truly difficult to find the region of interest (ROI). Thus, the developed diagnostic algorithm is developed to directly detect the ischemic in PF slices without concerning on the ROI segmentation.
5. Two-dimensional (2D) axial NECT brain slices which are stored in DICOM format with 512×512 resolutions have been used as the training, validation and testing dataset.

6. The diagnostic algorithm and GUI are developed using MATLAB R2019b toolbox as the software tool and Intel® Core ™ I7-7500U processor with 2.90GHz CPU and 8GB RAM as the testing platform.

1.5 Research Contributions

This study focuses on the development of algorithm to solve primary problem of ischemic stroke detection in PF such as poor sensitivity, inaccurate manual diagnostic and loss of gray-white matter differentiation while subside the traditional image processing. This study introduces an improved Xception model for the classification of ischemic in PF slices. The combination of the dropout method, as well as convolutional and max-pooling in the Xception model has shown to be less prone to overfitting than the original Xception model. To the best of author knowledge, this is the first approach which has been introduced for Xception model. Moreover, the advantage of introducing a classification network before detection is to reduce false localisation issue in the subsequent stage, in which the detection network focuses only on abnormal slices of PF.

A new approach in the detection stage is constructed by using hybrid of improved Xception model and YOLO V2 detector. In the newly proposed scheme, a number of detection sub-networks are compared. Max-pooling layer is integrated into each of the sub-network to further reduce the training loss. Although several detectors are reported in the literature, this work employs YOLO V2 detector due to its capability of performing high detection performance in medical image applications. Overall, the developed diagnostic algorithm is beneficial to facilitate radiologists in clinical emergency settings by integrating DL methods. Despite all efforts, no system or method today can provide a specific detection of ischemic in PF. Therefore, this has been a significant achievement of the work contained in this thesis.

1.6 Thesis Outline

The structure of this thesis is organised as follows:

Chapter 1 begins by discussing a brief background of this research. The problems in conventional ischemic diagnosis are identified and explained. The

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