EXTENDED DEVELOPMENT OF A COMPUTER AIDED DETECTION (CAD) SYSTEM FOR BRAIN BLEEDS IN CT

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ABSTRACT

Computer aided detection Computer aided detection (CAD) is a tool developed to assist radiologist interpretations from diagnostic modalities to decrease observational oversights or false negative rates. With CAD, radiologists able to use the computer output as second opinion, where the final decisions is still made by a human. One possible CAD usage is the detection of brain haemorrhage or in general terms brain bleed make it potentially useful in detection of brain bleed bleeds as a first-line screening tool, particular in emergency cases which occur outside regular working hours. Previous study by Leong show the useful of CAD system but her study is not fully automated. Thus the main objective of this study is to implement an automatic algorithm to previous algorithm to make it fully automatic system. In this study, 227 volumes of brain CT images were used to develop and validate the CAD. The new develop algorithm is set to register image of brain patient in order to determine the rotation angle for brain realignment. The new rotation angle obtained is compare with previous study to evaluate the differences. Then the new rotation angle is used to detect bleeding in the patient and evaluate the performance of the new algorithm. The algorithm for bleed detection consist of image processing to separate brain from the skull, rotation and realignment of the brain for mid-sagittal plane determination which used in bleeding detection. Final output of the algorithm summarise the bleeding detection for all patient in an excel file. The result obtained in this study show statistically difference in rotation angle between the new and previous study. Overall performance for new algorithm gives a sensitivity, specificity and accuracy for training 74%, 68.1% and 70.6% respectively and 84.6%, 67.1% and 73.4% respectively for the validation set. To be concluded, the new algorithm decreased the performance of the previous CAD system slightly but for a transition from manual to fully automatic, the

decrease is not very big. Having said that the new algorithm still needs improvements so that the CAD able to perform better.

ABSTRAK

Pengesanan berbantukan komputer (CAD) adalah alat yang dibangunkan untuk membantu tafsiran radiologi dari modaliti diagnostik untuk mengurangkan kecuaian pengamatan atau kadar negatif palsu. Dengan CAD, ahli radiologi dapat menggunakan output komputer sebagai pendapat kedua, di mana keputusan akhir masih dibuat oleh manusia. Salah satu penggunaan CAD yang boleh diaplikasikan adalah pengesanan pendarahan otak menjadikan ia berpotensi sebagai alat pemeriksaan talian pertama dalam mengesan pendarahan otak, khususnya dalam kes-kes kecemasan yang berlaku di luar waktu kerja. Kajian terdahulu oleh Leong menunjukkan berguna sistem CAD walaubagaimanapun kajiannya tidak dilakukan sepenuhnya secara automatik. Oleh itu objektif utama kajian ini adalah untuk mengaplikasikan algoritma automatik kepada algoritma terdahulu untuk menjadikannya sistem automatik sepenuhnya. Dalam kajian ini, 227 imej CT otak digunakan untuk membangun dan mengesahkan CAD. Algoritma baru yang dihasilkan telah ditetapkan untuk mendaftar imej otak pesakit kepada imej templat untuk menentukan sudut putaran bagi penyusunan semula otak. Sudut putaran baru yang diperoleh dibandingkan dengan kajian sebelumnya untuk menilai perbezaan. Kemudian sudut putaran baru digunakan untuk mengesan pendarahan otak dialami pesakit dan menilai prestasi algoritma baru. Algoritma untuk pengesanan pendarahan otak terdiri daripada pemprosesan imej untuk memisahkan otak dari tengkorak, putaran dan penyusunan semula otak untuk penentuan satah sagital tengah yang digunakan dalam pengesanan pendarahan. Hasil akhir algoritma merumuskan pengesanan pendarahan untuk semua pesakit dalam fail excel. Hasil yang diperoleh dalam kajian ini menunjukkan perbezaan statistik dalam sudut putaran antara kajian baru dan terdahulu. Prestasi keseluruhan untuk algoritma baru memberikan kepekaan, spesifikasi dan ketepatan untuk latihan masing-masing 74%, 68.1% dan 70.6% dan 84.6%, 67.1% dan 73.4% untuk set pengesahan. kesimpulannya, algoritma baru menurunkan prestasi

sistem CAD terdahulu sedikit tetapi untuk peralihan dari manual ke sepenuhnya automatik, penurunan itu tidak terlalu besar. Oleh itu, algoritma baru masih memerlukan penambahbaikan supaya sistem CAD dapat beroperasi dengan lebih baik.

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Muhammad Illyas B Abdul Muhji

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LIST OF SYMBOLS AND ABBREVIATIONS

CAD	:	Computed Aided Detection
CT	:	Computed Tomography
MRI	:	Magnetic Resonance Image
PET	:	Positron Emission Tomography
ICH	:	Intracranial Haemorrhage
IPH	:	Intraparenchymal Haemorrhage
AIH	:	Acute Intra Haemorrhage
HU	:	Hounsfield Unit
DBE	:	Detect Before Extract
FOV	:	Field of View
DICOM	:	Digital Imaging and COmmunications in Medicine
UMMC	:	University Malaya Medical Centre
CPU	:	Central Processing Unit
θ	:	Angle of Rotation
3D	:	3 Dimension
2D	:	2 Dimension
TP	:	True Positive
TN	:	True Negative
FP	:	False Positive
FN	:	False Negative
α	:	Critical Value

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CHAPTER 1: INTRODUCTION

1.1 Background

Computer aided detection (CAD) is a tool developed to assist radiologist interpret diagnostic results. The eventual aim is to decrease observational oversights or false negative rates (Castellino, 2005). It is not necessary for the computer performance to be better than the physicians, instead complementary to the physicians. With CAD, radiologists able to use the computer output as a “first screening” or “second opinion”, where the final decisions is still made by a human (Doi, 2007). The application of CAD has extended to many types of imaging modalities like ultrasound, computed tomography (CT), mammography, magnetic resonance imaging (MRI), and positron emission tomography (PET) (Rodríguez et al., 2016).

One possible CAD usage is the detection of brain haemorrhage or in general terms brain bleed. Brain bleed is a condition when there is bleeding occurring around the brain caused by trauma, high blood pressure, drug abuse, aneurysm etc. CAD is potentially useful in detection of brain bleed bleeds as a first-line screening tool, particular in emergency cases which occur outside regular working hours.

1.2 Brain Bleed: Overview

Brain bleed or brain haemorrhage is a condition where there is presence of bleeding at the brain region. This may be caused by trauma, high blood pressure, drug abuse, aneurysm, etc. The bleed can be inside the skull where it is known as intracranial haemorrhage, or within the brain where it is known as intracerebral haemorrhage, or a rupture of the blood vessel within the brain known as haemorrhagic stroke. Haemorrhage can lead to brain damage and can be lethal to the patient.

In order to diagnose brain bleeds, computed tomography (CT) is usually performed as it is fast and able to show basic characteristics of hematoma including the location, midline shift, existence of oedema and development of mass effect (Caceres and Goldstein, 2012).

Figure 1.1 CT slice showing presence of bleeding (Caceres and Goldstein, 2012)

ICH as mention before is characterized by the bleed location on brain.it can be outside the skull known as extraxial bleeding or on the brain known as intraaxial bleeding (Chan, 2007). Intraparenchymal haemorrhage (IPH) also known in general intracerebral haemorrhage is a type of intraaxial bleed, a condition where presence of non-traumatic bleeding into the brain parenchyma. It appear as hyperdense haemorrhage inside the cranial centred within the basal ganglia, occipital lobe or cerebellum (Heit et al., 2017).

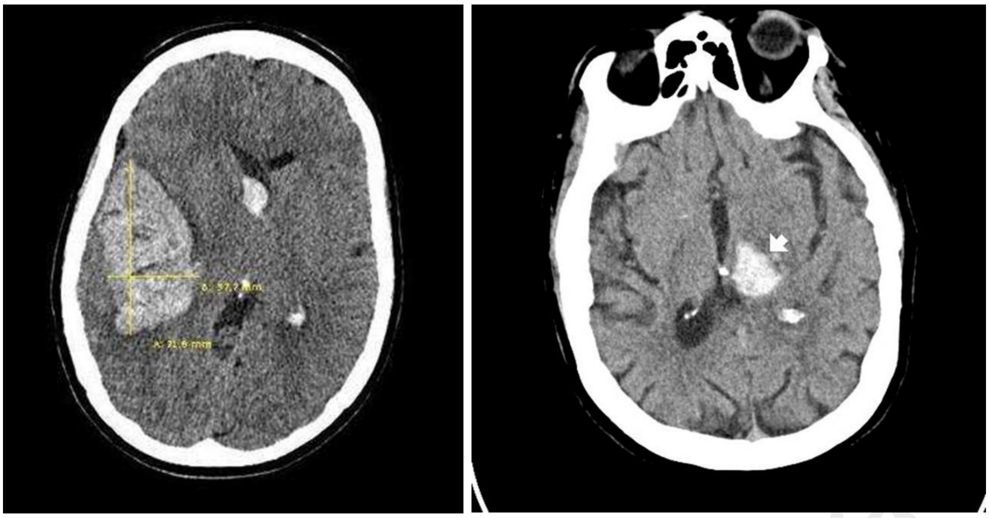

Figure 1.2 Various CT slices showing presence of intracerebral bleeding (hyperintense regions) (Caceres and Goldstein, 2012).

1.3 Objective

The objectives of this research are to:

1. Implement an automatic alignment algorithm to align CT images of the brain to a common reference alignment
2. Integrate the automatic alignment algorithm to the existing semi-automated bleed detection algorithm, thus making it fully-automatic.
3. Assess the impact of the automatic alignment algorithm on the overall performance of the existing bleed detection algorithm.

CHAPTER 2: LITERATURE REVIEW

In the era of computerization a number of human works have been replaced or augmented with efficient and convenient automated artificial intelligence technologies. In the medical field, such technologies are usually not for replacement, rather to assist the physician for a better treatment. CAD is a technology capable for detection of diseases and lesions. It has become part of routine clinical practice and is increasingly used for quantification and decision support as well as for detection and interpretation of diseases of various organs and the whole body (Nowinski et al., 2014). The aim of Computer-aided detection systems is to mark regions of an image that may reveal specific abnormalities and are used to alert clinicians to these regions during image interpretation. (Petrick et al., 2013). In this project we tackle the specific task of CAD for fully automatic brain bleed detection in CT images.

Many previous studies have been done to determine the usefulness of the CAD system in the detection of the brain bleed. A selection of published work is summarized in Table 2.1.

Table 2.1 Summary of various method used for CAD study on brain haemorrhage.

Research	Method	Cases	Result
Chan (2007)	**Thresholding and morphological operation** -Extraction of intracranial region -Preprocessing (median filtering, adjustment for cupping artefact) -Realignment -Identification of AIH (top-hat transformation and symmetry)	186 cases: <u>Training cases</u> 40 with AIH 80 control <u>Validation cases</u> 22 with AIH 44 control	<u>Training</u> Per patient basis: Sensitivity = 95%; Specificity = 89% Per lesion basis: Sensitivity = 84% <u>Validation</u> Per patient basis: Sensitivity = 100%;

			Specificity = 84% Per lesion basis: Sensitivity = 84%
Hara et al. (2007)	**Skull contour method** -separate the brain from the skull using thresholding technique at 84 HU -midline was determined -Normalization for the brain for construction of brain CT model -scoring the abnormalities using mean and standard deviation value	68 brain CT image 15 abnormal 53 normal brain	
Liu et al. (2008)	**Region splitting method** Stage 1: Split slices into encephalic region and nasal cavity Stage 2: Detect bleed (on encephalic region only) -Haar wavelet transform -Reconstruction -Feature extraction	493 cases (11011 images)	Accuracy = 80% sensitivity = 88%
W Zaki et al. (2009)	**Symmetry and rule-based abnormality detection** -Extraction of intracranial region (Binary coherent vector) -Calculation of axis of symmetry and realignment of brain -Calculation of largest area, AL and number of areas > 1/3 AL -Rule-based abnormalities detection (area, centroid)	20 abnormal images 80 normal images	Sensitivity = 100% Specificity = 91.25%
B.Srikanth et al. (2012)	**Detect-Before-Extract (DBE) method** -image processing -detection of midline symmetry using linear regression model (H-MLS model) -abnormal classification for brain scan images (histogram technique)	15 patients CT images 6 normal 9 abnormal	100% sensitivity 90% accuracy

Leong (2015)	-Extraction of brain -Realignment of brain -Determination of midsagittal plane -Detection of bleed	227 Patient CT images 87 abnormal 140 normal	**training set** sensitivity = 77.6%, specificity = 76.8% accuracy = 77.1% **validation set** sensitivity = 71.1%, specificity = 78.9% accuracy = 76.1%

It is noted that in five of the six listed works, a crucial step in the algorithm is some form of automatic detection of the left-right midline or mid-sagittal plane of the brain, either through global realignment of the head, or direct detection of the midline. This is because a common technique in brain bleed detection is via utilization of the left-right symmetry of the brain. I.e., brain bleeds are usually only dominant on one side of the brain, and may be detected via a left-right brain comparison. Thus, in order to determine the mid-sagittal plane, there are various method can be used to detect the angle rotation and realign the brain in an upright position.

Chan (2007) method utilizes the anatomy of the brain showed in CT image to find mid-sagittal plane. Base of anterior cranial fossa is located in this study as it correlates with the location lateral ventricle since it appears symmetrically at the midline. The slice contained bulk image of lateral ventricle is selected and the region is binarized and rotated at its centroid to a certain angle ranges. the mirror image is subtract to find different in the image and the rotation angle with lower differences is selected as the angle of mid-sagittal plane. Figure 2 show the flow of mid-sagittal plane determination. In this study, selection of slice containing the whole body of lateral ventricle is selected automatically. After detection of the plane, another alignment is done manually to verify the location of the plane as it may be inaccurate due to several factor.

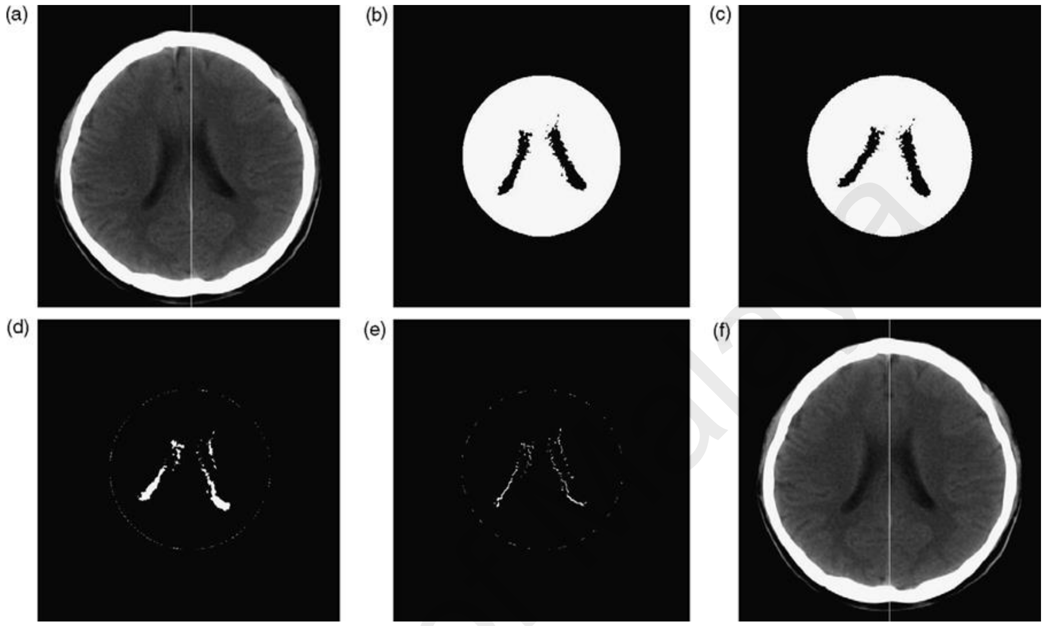

Figure 2.1 Flow of rotation angle determination. Begin with selecting slice containing lateral ventricle (a), binarized (b), rotated (c) and subtracted to find the lowest different at the rotation angle (d) (Chan, 2007).

Another method used to get the rotation angle is first by determining the principle axis of intracranial which used by W Zaki et al. (2009) in their studies. The axis obtained by calculating the lowest moment of straight line which lies along the maximum distance across the coordinate of mass centre and its angle. Meanwhile the rotation angle is obtained by simply bisecting the principle axis angle. The image is rotated at rotation angle value to get an upright brain image so that the symmetrical line can be generated. Figure 2.2 illustrate the whole process of rotation angle determination.

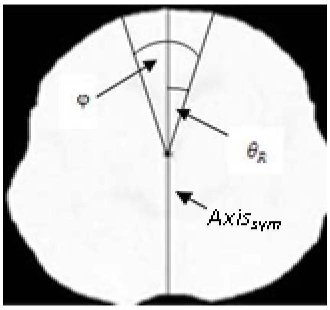

Figure 2.2 Bisecting principle axis angle, φ to get rotation angle, θ_R (W Zaki et al., 2009).

Study by Ali et al. (2012), introduced method for midline plane detection via image registration for comparative analysis of patient's image slices. The study suggest analysing patient image slices via synchronize viewing. The techniques comprise of approximate transform correcting the global differences in position, orientation and shear between the reference and the test volume. Then elastic registration applied to show both global and local deformations. The system is done fully automatic and robust for aligning any series of body part image with respect to a reference image.

I now focus specifically on Leong (2015) a previous Medical Physics student who developed and tested a semi-automatic brain bleed detection algorithm. Her method comprised two stages: pre-processing and bleed detection. In the pre-processing stage, the brain was automatically segmented from the skull, then manually rotated and realigned so that the mid-sagittal (midline) plane was vertically aligned in the centre of the image. Bleeds were detected by dividing the processed image into left-right halves, and the two halves were subtracted for comparison, to highlight any abnormalities or disproportion on each halve. Further morphological operations were performed to remove noise and edge artefacts. The results obtained for her code yielded sensitivity of 77.6%, specificity of 76.8%, and accuracy of 77.1% for the training set, and sensitivity of 71.1%, specificity of 78.9%, and accuracy of 76.1% for the validation set.

In this project, an automatic algorithm for realignment and repositioning of CT brain images is developed and tested, the aim being to enable subsequent algorithms to analyse the left-right brain symmetry for automatic brain bleed detection. The realignment algorithm was also integrated with the previously developed semi-automatic brain bleed CAD system (Leong, 2015), so as to make the system fully-automatic.

CHAPTER 3: METHODOLOGY

3.1 Materials

Two hundred and twenty seven (227) volumes of CT images were obtained from the previous study of automatic brain bleed detection. These were acquired from University Malaya Medical Centre (UMMC), from the emergency department and biomedical imaging department between 22 February 2015 to 10 April 2015. All images are in Digital Imaging and COmmunications in Medicine (DICOM) format, with of 512 × 512 pixel dimension. Slice thickness varies between 1.25 mm to 3.0 mm among volumes. All images were acquired using 120 kVp, except 3 volumes of images of children were acquired using 100 kVp, and 1 infant acquired using 80 kVp. The field of view (FOV) is varied between volumes and ranged between 179 mm to 350 mm, , reflecting varying head size. The positioning of the head within each volume is also not constant, including images acquired superior-to-inferior and vice versa.

Eighty seven (87) out of the 227 volumes contain at least one acute intracranial bleed. All volumes were divided randomly into two sets, namely the training set and the validation set. The training set contained 118 volumes where 49 of them contain acute bleed while the rest is normal. The validation set consisted of 109 volumes where 38 of them contain acute bleed and 71 are normal. Diagnosis of all cases was made by at least one radiologist from UMMC and is taken as the gold standard in this study.

All the images obtained were transferred and processed on a Personal Computer with Intel (R) Core i5 -4200U CPU @ 1.60 GHz 2.30 GHz processor, running on Windows 10 operating system. The algorithms were written using MATLAB 2017a (The MathWorks, Inc., Natick, MA, USA).

3.2 Overview of Previous Method

In the previous study described in chapter 2 (Leong, 2015), the brain bleed detection algorithm is considered to be semi-automatic. This is because the algorithm is dependent on a properly aligned brain to detect midline symmetry, but it did not perform automatic rotation and realignment of the brain. Instead it required a manually specified rotation angle. I.e., the user had to calculate the angle manually.

In this study, I develop an automatic realignment method for brain CT images based on image registration. Two main steps are involved: template preparation and automatic registration.

3.3 Method

3.3.1 Template Preparation

Template preparation is to create a combined template of representative brain images to act as the reference or fixed image for all other images to be registered against. The images chosen for the template were selected based on (1) having a midline angle close to vertical, (2) no presence of bleeds, and (3) having a relatively conventional brain shape. Only 2D registration is used, so only a single 2D slice is obtained from each selected patient.

3.3.2 Patient‘s Brain CT Image Selection

Ten patients deemed to meet the above criteria were manually selected from the training set, and a single slice representative of the midbrain was extracted from each volume. Out of these 10 slices, one slice was identified to have the best overall representative quality, with midline angle of 0 degrees. This slice was selected to become a fixed base for the other slices. The other nine slices from the rest of the selected patients were then automatically registered to the fixed base using a similarity transformation (translation, rotation, and scale) and using mean squared error as the similarity metric.

3.3.3 Extraction of Intracranial Region

Preliminary to image registration, all selected image brain was segmented to separate the cranial region from the grey matter region. Thus the images only contain the grey matter and soft tissue. In the process, the pixel value is converted to Hounsfield Unit (HU) for global thresholding. Then the images undergo morphological operation to remove small remaining details from the cranial part. At the end of the process brain image containing information on the grey matter is obtained. Figure show the brain image after segmented from the intracranial region.

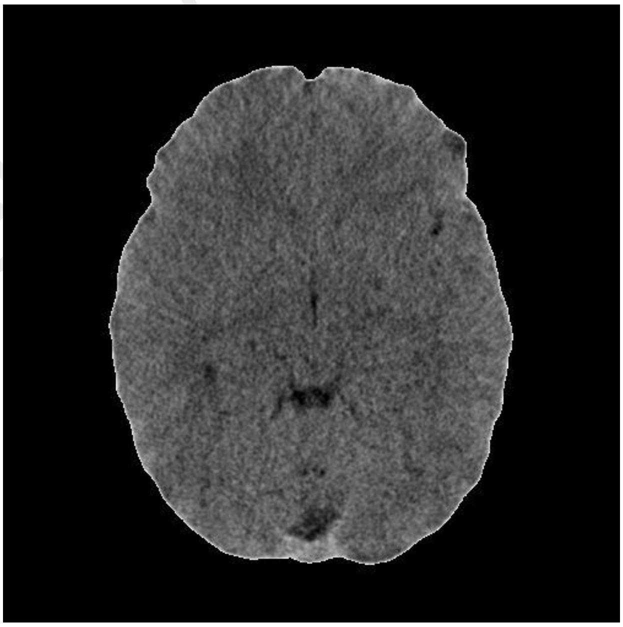

Figure 3.1 Brain image separated from the skull.

3.3.4 Registration of Selected Patient's Brain Image

After the brain is segmented from the intracranial region, all nine slices were registered to the fixed base; the ten images were averaged via arithmetic mean to obtain the final 2D template image. Registration used is similarity registration which transforms the slices in a manner of translation, rotation and scale.

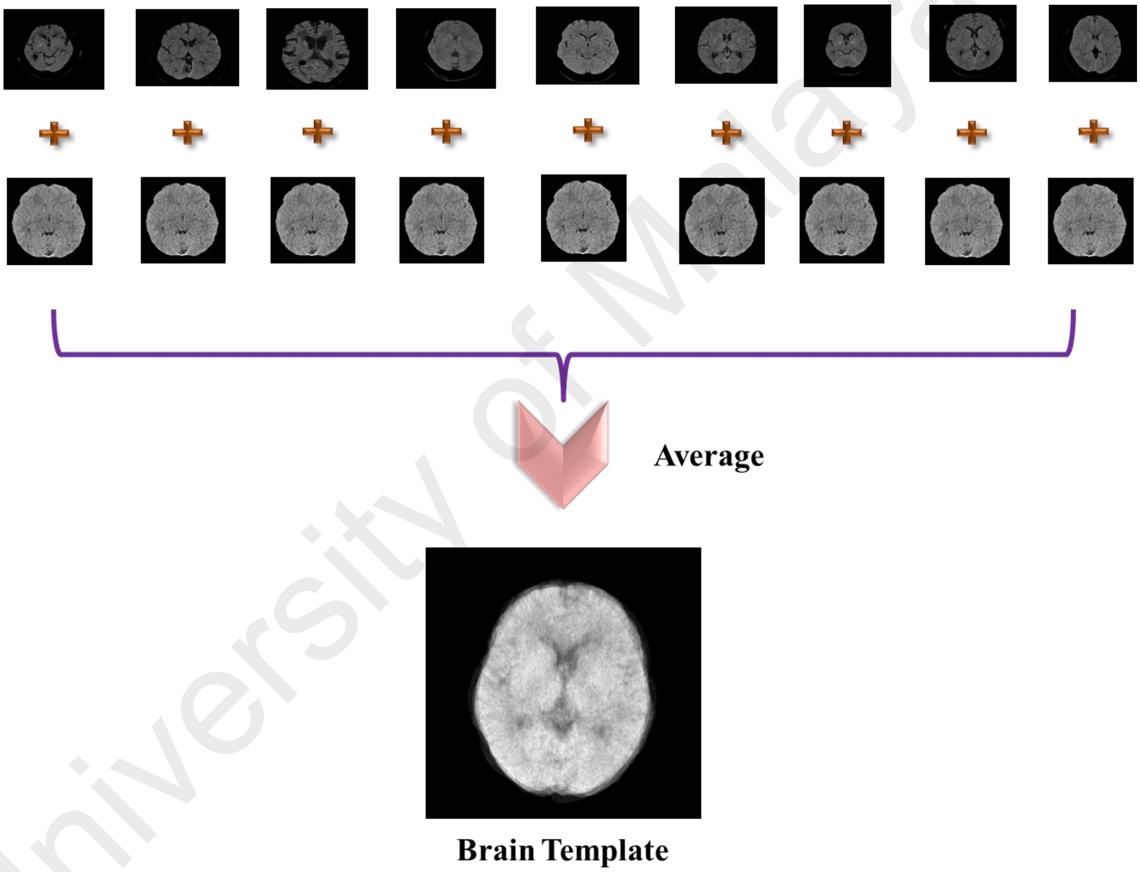

Figure 3.2 Brain template constructions

The objective of this template construction is to get an encephalic region with constant shape and without any tilted. Hence the CT slices will undergo rotation and translation so it will match with the template. The brain realignment is done for each patient for both set. The patient's brain CT was registered to the brain template and done in 2D since the template is not in 3D volume. In regards of that, only five slices in the middle of the brain CT volume was automatically selected and registered.

3.3.5 Automatic Brain Registration

In order to rotate the image, patient's image was registered to the template created in 2D manner instead of 3D. In other word, to describe the registration process, the selected CT slice will be overlap with brain template and undergo rotation and translation the slice so that it will be in the same position as brain template. Prior to that, 5 slices in the middle was chosen from out of the patient total slice number. The algorithm created was set to find the middle slice and take 2 slices both from upper and lower from the middle. Then the slices were segmented to remove the cranial part of the image so that only the brain part that was registered. Each selected slices that registered mostly have different angle from another. Therefore a median angle value is selected to be the angle of rotation, Ɵ. Then, the Ɵ value determined was tabulated and compared with previous study Ɵ.

To do this, the full 3D volume for each patient was first loaded, and five slices from the middle of the volume were extracted. E.g., if the patient volume consisted of 60 slices, then slices 28-32 would be selected, and assumed to be in the vicinity of the midbrain. Brain extraction identical to the previous section would be applied, and each of the five slices would be separately registered to the template using similar transformation parameters and similarity metrics. The angle of rotation, Ɵ was extracted from the final transformation matrix, and the median rotation angle of the five slices was calculated and chosen as the final angle used.

3.3.6 Rotation Angle, Ɵ Statistical Analysis

Since the algorithm registered the entire patient brain image automatically, there is no repeating process for each of next patient's brain image manually. At the end of the automatic registration process, it generates the median Ɵ for each patient volume. The Ɵ is transfer in an excel file for further analysis the difference between the angle obtained in this study and the previous study. A normality test which is known as Kolmogorov-Smirnov test was carried out on new and previous rotation angle for both set to determine the normal distribution on each sample. Then pair statistical analysis is used to evaluate the different of Ɵ obtained for this study to the previous one depending on the distribution of the sets.

3.3.7 Brain Bleed Detection

In order to test the effect of the automatic realignment algorithm, the automatically determined rotation angle, Ɵ was used to replace the original manually determined angle used by the semi-automatic brain bleed detection algorithm (Leong, 2015) in both the training and validation sets. No other change was made to the brain bleed detection algorithm. Table 2 summarise on the flow of previous algorithm by Leong (2015) and Figure 3.1 show the flowchart of overall process.

Table 3.1 Brain detection algorithm summary by Leong (2015)

Steps	Methods and Parameters Used	Purposes
Extraction of brain	• Global thresholding : 10HU - 100HU • Morphological operation: opening with 'disk' erosion with 'disk' • Statistical selection: voxel >1000000	To extract the intracranial region and to remove the skull, scalp and other irrelevant structures.
Realignment of brain	• Rotation of image: angle predetermined manually 2D rotation done for each slice	To realign the extracted brain so that the midsagittal plane can be found easily.
Determination of midsagittal plane	• Region properties: 'centroid'	To locate the midsagittal plane.
Detection of bleed (part 1)	• Preprocessing: median filtering • Left-right subtraction: Divide the brain along midsagittal plane Flip the left half Subtract right half from left half • Thresholding: 20HU - 60HU, for left bleed -20HU - -60HU, for right bleed • Morphological operation: opening with 3D 'diamond' shaped structural element of radius 2. • Reconstruction of mask from the left and right halves	To produce a mask which indicates the possible acute bleed by the left-right differences in density (using the idea of symmetry).
Detection of bleed (part 2)	• Global thresholding: 45HU - 100HU • Morphological operation: opening with 3D 'diamond' shaped structural element of radius 1.	To produce a mask which indicates the possible acute bleed by the density of acute bleed alone.
Detection of bleed (part 3)	• Intersecting masks from Part 1 and Part 2. • Statistical selection: Pick volume > 500 mm^3	To produce a mask which can indicate the acute bleed by combining criteria set in Part 1 and Part 2 of bleed detection.

The end process of the algorithm produced excel file of the bleed detection information for all each set. The summary of the bleeding was use and compare with the standard (reference) and previous result. Binary system is used to categorize the bleeding where presence of bleed as 1 and non-bleed as 0. The performance of new algorithm is evaluated using sensitivity, specificity and accuracy which can be calculated as follow:

$$sensitivity = \frac{TP}{TP+FN} \times 100\% \quad \text{… Eq. 1}$$

$$spesificity = \frac{TN}{TN+FP} \times 100\% \quad \text{… Eq. 2}$$

$$accuracy = \frac{TP+TN}{TP+TN+FP+FN} \times 100\% \quad \text{... Eq. 3}$$

Where:

True Positive (TP) = the algorithm detect at least one region as bleed in the patient with bleeding.

True Negative (TN) = the algorithm did not detect any bleed in the patient without bleeding.

False Positive (FP) = the algorithm detect one or more bleed in the patient without bleeding.

False Negative (FN) = the algorithm did not detect any bleed in the patient with bleeding.

Each of these classifications is defined according to the ability of the algorithm detecting the bleed and off to the standard. Binary system was also used to enumerate the classes for further calculation of the evaluation. In other words if the code detect bleed in patient with actual bleeding, the TP will be enumerate as 1 while other is 0 and so on for other cases. The total of each classes and the performance is calculated, tabulated and compare with previous result to see any changes occur for the new algorithm.

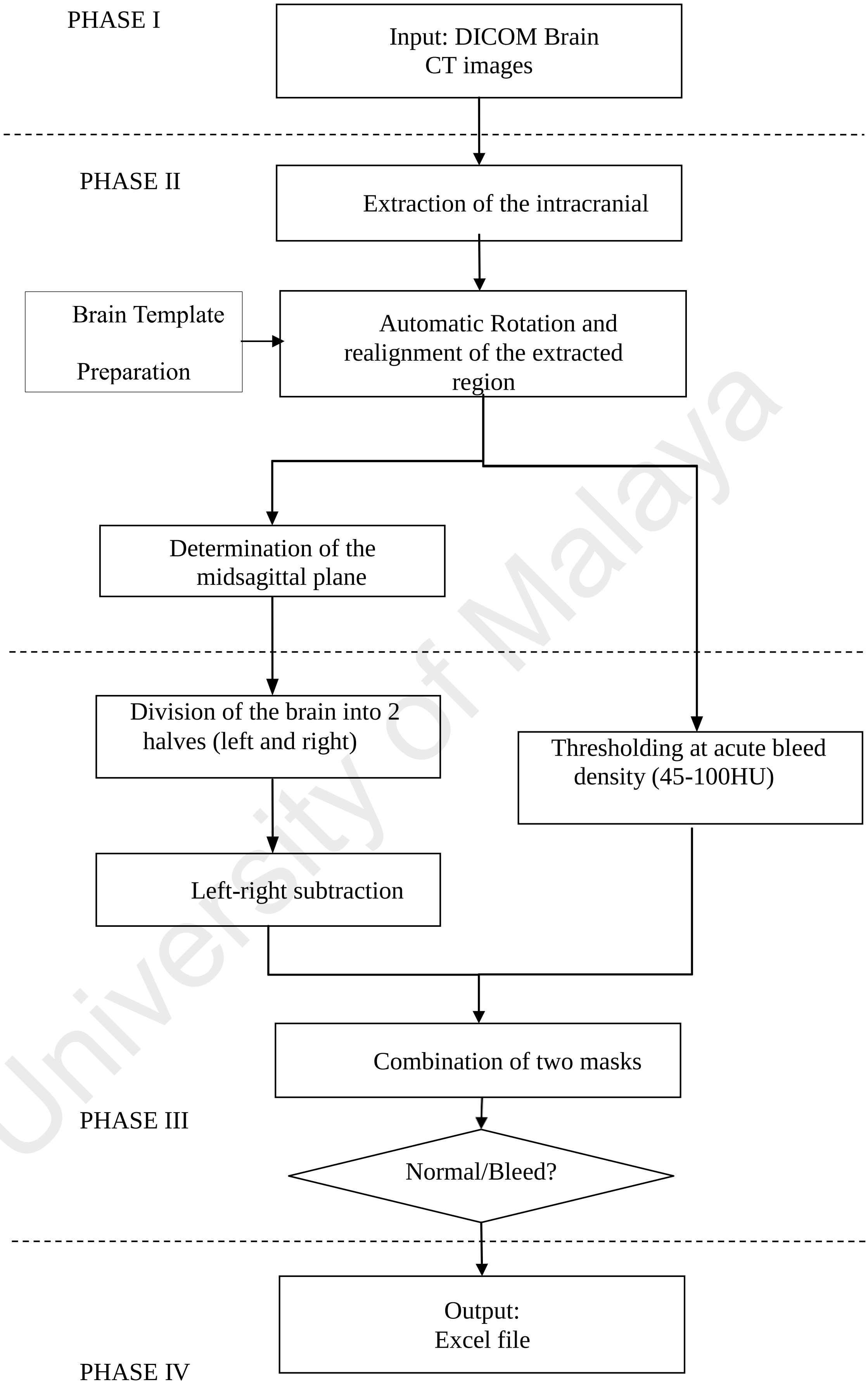

Figure 3.3 Flowchart of new algorithm detecting the brain bleed.

CHAPTER 4: RESULTS AND DISCUSSION

4.1 Angle of Rotation Analysis

The main purpose of this study is to make the brain bleed algorithm fully automated by replacing the manually determined brain rotation angle, ϴ, with an automatically determined rotation angle. Table 2 show the descriptive statistic of both new and previous ϴ in training and validation set. Table 4.1 shows the descriptive statistics of both the new (automated) and previous (manual) ϴ in both the training and validation sets.

Table 4.1 Descriptive statistics for rotation angles ϴ in the training and validation sets.

Set	Study	Descriptive Statistic				
		Mean	Mean Difference	Standard Deviation	Minimum	Maximum
Training	New ϴ	-2.69	-2.18	4.63	-14.2	16.8
	Previous ϴ	-0.51		4.01	-14.0	12.0
Validate	New ϴ	-2.82	-2.88	4.67	-13.9	12.4
	Previous ϴ	0.06		3.84	-8.00	10.0

Table 4.2 Descriptive statistic result for absolute difference of the θ in both set

Set	Training		Validate	
Descriptive Statistics	positive new θ	positive previous θ	positive new θ	positive previous θ
Mean	3.97	3.12	4.12	2.94
Mean difference	0.847		1.18	
Median	3.00	3.00	3.00	3.00
Minimum	0.00	0.00	0.00	0.00
Maximum	17.0	14.0	14.0	10.0

In the set of results obtained for both θ in new and previous study contain negative sign indicating the direction of the rotation during transformation. All the sign was eliminated and analyse for mean absolute difference as shown in Table 4.2. Comparing to the mean difference in table 4.1, the mean difference is in negative value.

Table 4.3 Kolmogorov-Smirnov normality test result on both training and validation set

Set	Rotation Angle, ϴ	P-value (two tail)	Distribution
Training	New angle	0.003	Not normal
	Previous angle	0.200	Normal
Validation	New angle	0.009	Not normal
	Previous angle	0.010	Not normal

Table 4.3 showed the result of normality test conducted on every sets of angle. From the table each set of angle have non-normal distribution except for the previous angle for training set. Therefore, the statistical analysis done for the next step used a non-parametric t-test known as Wilcoxon Signed Rank test to evaluate the differences between the new and previous study.

Table 4.4 Wilcoxon Signed Rank test result on both training and validation set

Set	Study	Wilcoxon Signed Rank Test			
		Standard deviation	N	P(T<=t) two-tail	z-Stat
Training	Previous ϴ - New ϴ	377.1	119	<< 0.05	5.03
Validate	Previous ϴ - New ϴ	330.7	109	<< 0.05	5.09

Table 4.4 summarises the Wilcoxon signed rank test to compare differences between the previous and new results. With α-value set at 0.05, the result shows a statistically significant difference between ϴ for both the training and validation sets. Hence, it can be concluded that there is a statistically difference between the rotational angle, ϴ determined manually and by the automatic algorithm.

Assume a $\pm 0.5^{\circ}$ angle difference to be negligible, then 13.5% and 8.3% results in the training and validation sets respectively were unchanged between the manual and automatic algorithm. Within these cases, the majority were of brains that were already effectively at a vertical angle. Figure 4.1 shows a sample brain image that was registered to the template with a similar angle as determined in the previous study.

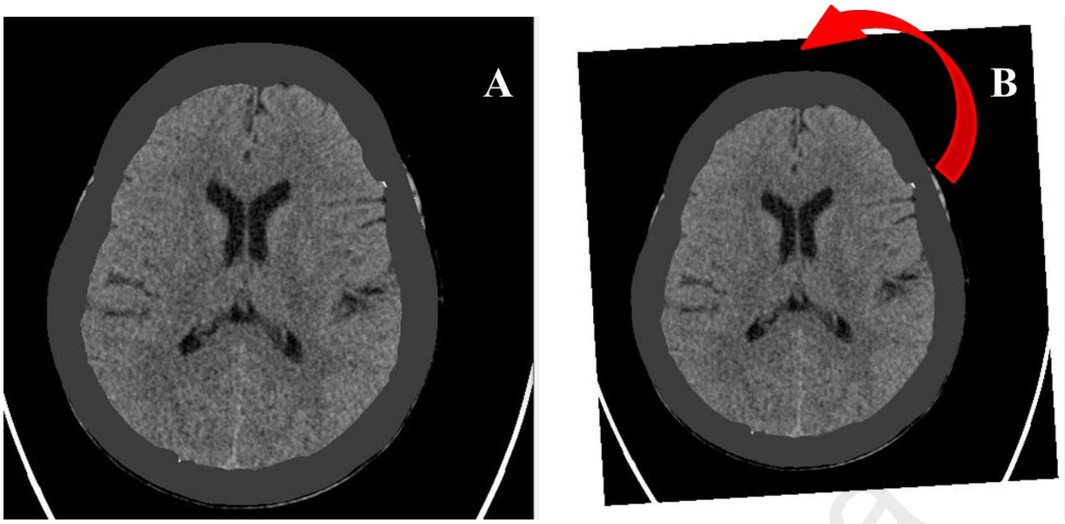

Figure 4.1 sample case where the automatically registered brain image resulted in a ϴ similar to the previous manual angle. Image A is the unregistered image. Image B is registered image, showing negligible change in rotation in image registered with ϴ detect similar to previous case

It is supposed the automated algorithm detect the same as manual because as mention before the previous study detects the ϴ so it becomes upright position. Therefore the ϴ detected by automated algorithm deviates so much from the original ϴ. But there also cases where image failed to register as expected resulting in error for determining the ϴ.

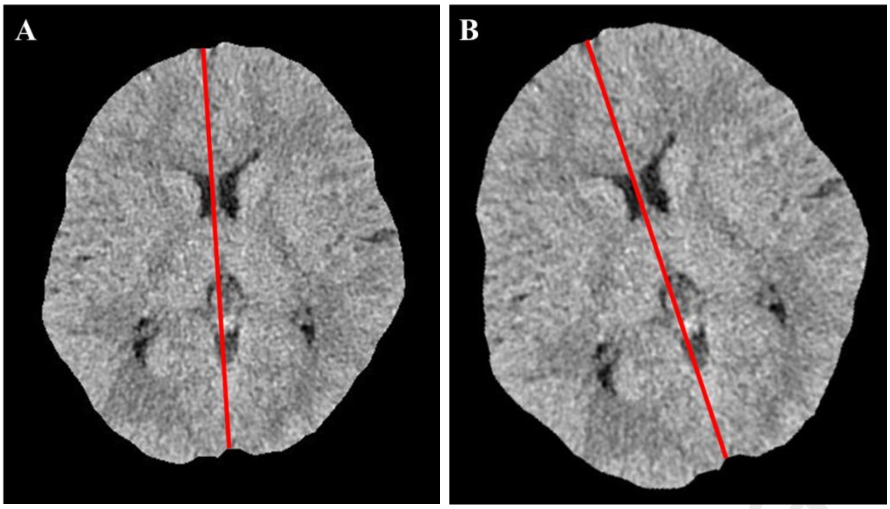

Figure 4.2 Registered images (B) demonstrate a significantly worse tilt compared to the original image (A).

Figure 4.2 shows an example of a failed automatic registration. The registered brain angle is significantly worse than the original image. The correct manual Ө for the upright position is -2°, however the automatic registration returned -17°. It is unclear what caused the misregistration. The deviation might be due to the registration algorithm matching internal details of the template rather than the overall shape and position.

A few factor can be considered contribute to the error such as template created contains averaged details from the selected brain images (Figure 4.3). These details should be utilized by the registration algorithm for proper alignment to the template image. It is possible that due to similarities or indistinct patterns, some details were being mismatched between the template and moving images, resulting in the registration error.

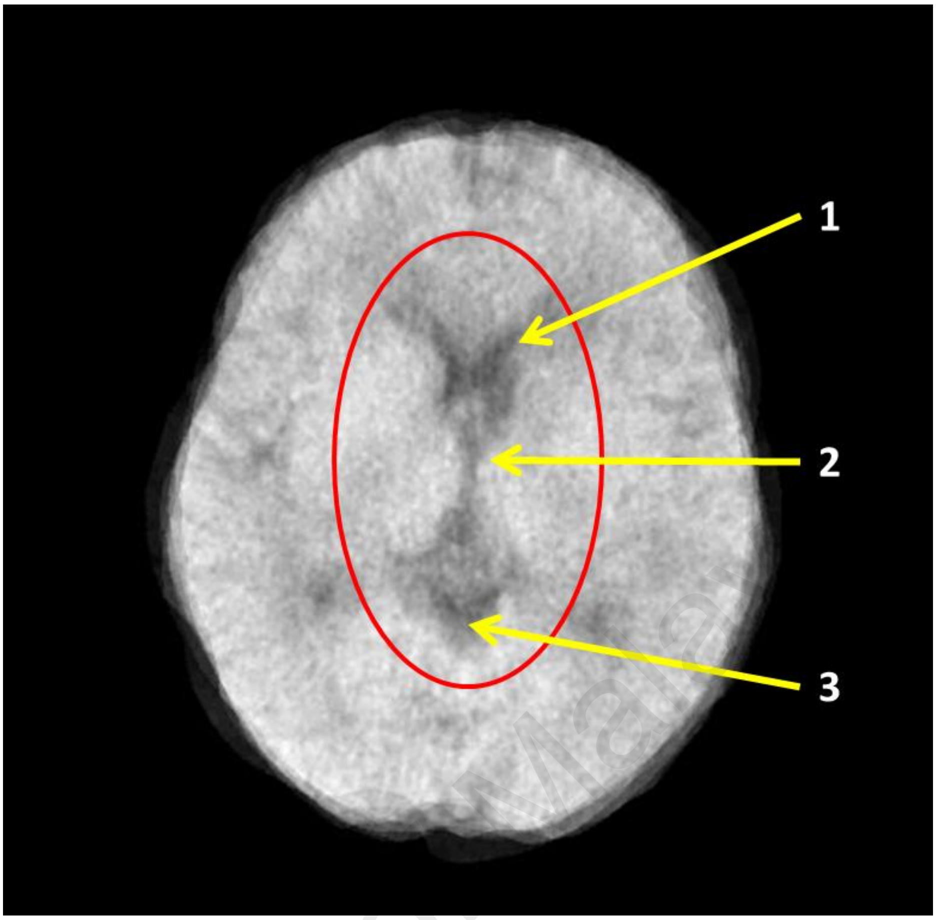

Figure 4.3 Red circle show the frontal horn (1), ventricle (2) and cistern (3) in the brain template.

Another factor affecting the registration is the brain geometry. The CT image numbering and slice coverage differs from patient to patient due to differences in anatomy and CT scan positioning. Figure 4.1 and 4.1 both show irregularities with the brain image from different patients, possibly due to different slice positioning. The algorithm only relies on a simple method to extract the mid-slice: the middle numbered image plus two slices below and above. Thus the algorithm may not be robust against irregularities on different geometry.

4.2 Performance of the Automatic Algorithm

The automated rotation angle algorithm was integrated into the previous semi-automated bleed detection algorithm (Leong, 2015). Evaluation of the performance of the automated bleed detection was repeated using sensitivity, specificity, and accuracy, calculated on a per patient basis for both the training and validation set. This means we count each patient as a single sample, regardless of the number of bleeds. In this study, only per patient basis is done because it is more clinically relevant for the desired purpose: screening of trauma cases after hours. The aim is to highlight patients that will be given priority to be read by a radiologist (Leong, 2015). The verification is done by the radiologist to decide the type of bleeds occurring in the patients. The sensitivity, specificity and accuracy are as described as in Eq. 1, Eq. 2 and Eq. 3.

Sensitivity tests the algorithm's ability to pick up bleeding patients. Specificity tests the ability of algorithm to rule out non-bleed patients correctly. While accuracy tests the overall ability of the algorithm to differentiate between patients with bleed and non-bleed patient (Baratloo et al., 2015). Table 4.4 shows and compares the performance of the algorithm for the new and previous study.

Table 4.5 Performance of automated algorithm compared with previous study

Set	Performance (%)	new study	previous study	Differences
Training	sensitivity	74.00	77.6	-3.60
	specificity	68.12	76.8	-8.68
	accuracy	70.59	77.1	-6.51

Validation	sensitivity	84.62	71.1	13.52
	specificity	67.14	78.9	-11.76
	accuracy	73.39	76.1	-2.71

As expected, there is a modest decrease in overall performance when using the automated rotation angle algorithm as opposed to a manual reading. However, in most cases the performance decrease is within 10%. Considering the intended purpose as a screening tool, sensitivity is the most relevant metric. Here, we see only a small drop in performance of -3.6% for the training set, and a surprising increase in performance of 13.5% for the validation set. It is unclear the reason for this unexpected improvement. The increases in sensitivity for validation set might be affected by the number of patient with no bleeding originally compare to training set contain quite a lot of patient with bleeding. For a transition from a semi-automatic, human involved process to a fully automatic system, the performance decreases can be said to be acceptable.

Automatic system would require larger numbers of training and test sets and better performance should be achievable. Although the accuracy to detect the rotation angle is not very good but the performance test shows that the bleed detection algorithm is robust, with results better than expected.

4.3 Future Work

Future work for improvement of the automatic rotation angle algorithm as well as the overall brain bleed detection algorithm includes:

1. Registration in 3D volume

   It is suggested to do 3D registration because the entire CT data can be registered as a single volume. It might also solve the issue of selecting the midslice image in 2D.

2. Picking a slice similar to the template

   When doing the registration, the algorithm should consider using a brain image similar to the template rather than just picking the midslice. This might be registering multiple slices separately, and then analysing the final registration quality metric or similarity metric.

3. Focus on the midline shift

   Midline shift is considered to be one of the pathology signs that may indicate brain bleed. Developing code to detect any changes in the midline may increase the performance of the automatic brain bleed detection system.

CHAPTER 5: CONCLUSION

A fully automatic rotation angle registration system was developed in this study replacing the manually determined system of the previous study. This turns the semi-automatic brain bleed detection system in the previous study into a fully automatic system that detects brain bleeds through the bilateral property of the brain. Despite its usefulness, the new fully automated brain bleed detection system has a lower overall performance compared to the previous system. The new sensitivity, specificity and accuracy are 74%, 68.1% and 70.6% respectively for the training set and 84.6%, 67.1% and 73.4% respectively for the validation set. The drop in performance is largely within 10%. For screening use, the drop in sensitivity is only -3.6% for the training set, and surprisingly improves by 13.5% for the validation set

In conclusion, the manual determination of the angle of rotation as used in the previous, semi-automated study is tedious and inefficient, especially when working with large sets of patient images. An automatic angle detection system makes the process easier and efficient, and enables unmanned screening of brain bleeds for trauma cases after working hours.

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