SEGMENTATION OF BRAIN VOLUMES FROM T2-WEIGHTED AND DOUBLE-INVERSION-RECOVERY MR IMAGES

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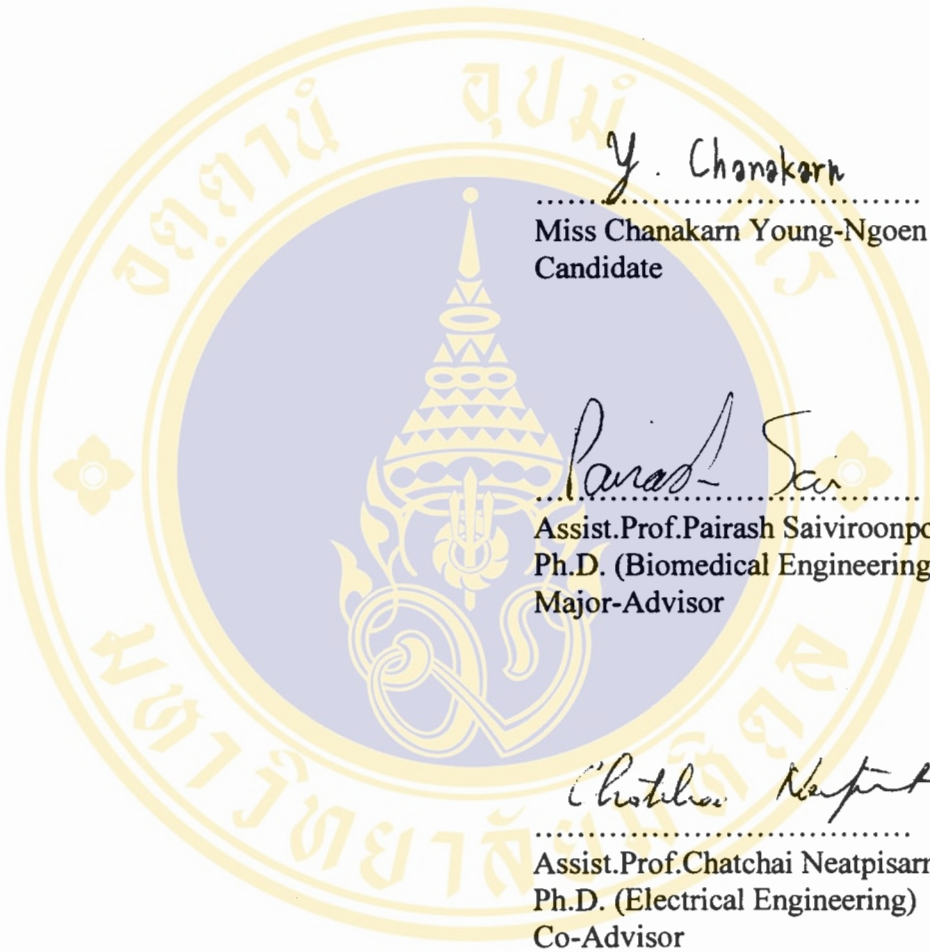

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SEGMENTATION OF BRAIN VOLUMES FROM T2-WEIGHTED AND DOUBLE-INVERSION-RECOVERY MR IMAGES.

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ABSTRACT

The purpose of this study was to validate a new segmentation technique that uses T2-Weighted and Double Inversion Recovery (DIR) MR images for segmentation of brain tissue volumes. White matter (WM) and gray matter (GM) tissue volumes were segmented from eight healthy volunteers. The 3D Slicer, open source software, was used as a semi-automated segmentation tool. Results from the proposed method (T2W+DIR) were compared to the reference method (GRE3mm) which was justified from the conventional method (GRE1mm). Pearson's correlation and Paired t-test were used for statistical analysis.

The overall segmented WM tissues demonstrated that there was a reasonable correlation between the proposed method and reference method (Pearson Correlation = 0.78). However, there was low correlation (Pearson Correlation = -0.40) in GM volumes and some cases were found to be highly different among methods, due to unclear tissue borders in the conventional and reference methods. The results of GM should be improved in reliability. The segmentation time was reduced in the proposed method.

In conclusion, the proposed method was valid in WM segmentation and reduced the segmentation time of the conventional method which is a benefit for the initial step of quantitative brain volume research such as in dementia studies. Further research should use larger sample sizes for statistical analysis or adjust image resolution and segmentation time, depending on study objectives.

KEY WORDS: SEGMENTATION / DOUBLE INVERSION RECOVERY / MRI / BRAIN VOLUMES / WHITE MATTER / GRAY MATTER

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การแยกส่วนปริมาตรสมองจากภาพเอ็มอาร์ชนิดทีทูและดับเบิ้ลอินเวอร์ชั่นรีคัฟเวอรี่

(SEGMENTATION OF BRAIN VOLUMES FROM T2-WEIGHTED AND DOUBLE-INVERSION-RECOVERY MR IMAGES)

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บทคัดย่อ

การศึกษานี้มีวัตถุประสงค์เพื่อตรวจสอบความสมเหตุสมผล ของวิธีการแยกส่วนปริมาตรสมองจากภาพเอ็มอาร์ชนิดทีทู (T2-Weighted) และดับเบิ้ลอินเวอร์ชั่นรีคัฟเวอรี่ (DIR) โดยทำการแยกส่วนปริมาตรสมองออกเป็นส่วนของเนื้อสมองส่วนขาว (White Matter) และเนื้อสมองส่วนเทา (Gray Matter) จากอาสาสมัครสุขภาพดี จำนวน 8 คน และนำผลของปริมาตรที่ได้เปรียบเทียบกับการแยกส่วนปริมาตรโดยใช้ภาพเอ็มอาร์มาตรฐานที่ใช้ในทางคลินิค โดยใช้ 3D Slicer เป็นเครื่องมือในการแยกส่วนและหาปริมาตรเนื่องจากเป็นซอฟแวร์ที่ให้ผลเป็นที่ยอมรับและใช้ในงานวิจัยอย่างแพร่หลาย จากนั้นจึงวิเคราะห์ข้อมูลโดยใช้ Pearson's correlation และ Paired t- test

ผลการหาปริมาตรของเนื้อสมองทั้งส่วนขาวและส่วนเทาได้ค่าใกล้เคียงกันทั้งสองวิธี โดยมีบางกรณีพบว่าผลของปริมาตรที่ได้จากวิธีที่นำเสนอในการศึกษานี้ จะให้ค่ามากกว่าเนื่องจากภาพที่ใช้ในวิธีมาตรฐานไม่สามารถแยกส่วนในภาพได้อย่างชัดเจน โดยเฉพาะในส่วนเนื้อสมองส่วนเทา จึงทำให้มีความแตกต่างของปริมาตรมากกว่าพบในส่วนขาว และในด้านเวลาที่ใช้ในวิธีที่นำเสนอให้ผลเป็นที่น่าพอใจ ทำให้สามารถลดระยะเวลาในการแบ่งส่วนจากวิธีมาตรฐานได้ โดยสรุปวิธีที่ใช้ในการวิจัยนี้เหมาะสำหรับใช้เป็นการแยกส่วนปริมาตรเบื้องต้นสำหรับงานวิจัย เนื่องจากจำนวนกลุ่มตัวอย่างในการวิจัยยังค่อนข้างน้อยในการวิเคราะห์ทางสถิติสำหรับในการวิจัยเพิ่มเติมนั้นควรเพิ่มขนาดและความหลากหลายของกลุ่มตัวอย่าง หรือสามารถปรับลดขนาดความหนาของภาพเอ็มอาร์เพื่อเพิ่มความละเอียดของภาพแต่จะทำให้เสียเวลาในขั้นตอนการได้ข้อมูลมากขึ้น จึงขึ้นอยู่กับวัตถุประสงค์ในการใช้งานต่อไป

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CHAPTER I

INTRODUCTION

1.1 Introduction

Magnetic resonance imaging (MRI) is a conventional imaging technique to assess of soft tissue anatomical structures as well as pathological changes. MRI can benefit not only for diagnosis propose but also for quantitative analysis. The post processing of MR images, therefore, pays a crucial role for separating each part of interested volume from stack of 2D cross section MR images. It is, however, important to use the proper techniques to extract the maximum information from the images and to answer the specific questions. The advantages and disadvantages of specific techniques must be considered, to minimize the risk of missing a diagnosis or incompletely reporting.

Segmentation, a classification process, is the most important and difficult part of post processing process for quantitative analysis. The process outcome is label of each region of interest in the pattern of label map to indicate its tissue structure. The current process has relied on manual tracing of 2D contiguous images of the whole brain. Manual segmentation is a tedious and time-consuming process. This problem is somewhat reduced by using automatic or semi-automate segmentation method. However, manual segmentation is still essentially employed for correcting of missegmentation result from the automatic process.

One of the open-source software for MR segmentation, 3D Slicer, is a collaborating project developed by MIT Artificial Intelligence Lab and Surgical Planning Lab at Brigham & Women's Hospital, an affiliate of Harvard Medical School. It provides a common research platform with basic functions and flexibilities for specific research. The software has been used actively in a variety of clinical researches including neurosurgical planning, investigation of Alzheimer's disease, multiple sclerosis, and schizophrenia. (Kikinis: 1992, Kapur et al: 1996, Killiany et al: 1999, Meier et al: 2003, and Liu et al: 2004). Since it has been widely used in research

worldwide included Siriraj Hospital, 3D Slicer is suitable semi-automatic segmentation tool, and reliable to perform brain tissue segmentation in this study.

3D gradient echo T1 weighted (3D GRE-T1W) MR volume image is one of the most utilizes protocol to obtain images for the MR segmentation. The image, however, is quite difficult for the classification of gray and white matter region in the brain due to its low contrast between these two parts. Recently, a new protocol, a double inversion recovery (DIR) sequence, has been introduced for such the task. The new imaging technique can provide very high contrast between these two regions, which can simplify the segmentation process (Redpath, 1994).

Most MRI examinations will involve an evaluation of both T1W and T2W images. T1W sequences use for anatomical study and T2W sequences best demonstrate pathological conditions because most inflammatory process appears bright in signal as a result of the increase water content.

There is a recently report on the manual volumetric segmentation of the brain based on landmarks into four different lobes which can be used as a protocol to segment the brain (Bokde et al: 2005). The segmented results can be implemented on 3D Slicer shown in Figure 1.1 the same as that protocol divided cortex of the brain into 4 major lobes: frontal, parietal, temporal, and occipital. The segmentation was manual define the lobar based on neuroanatomical reference book (Patel et al: 1997).

In this study, the segmentation results from the extraction of the two cerebral brain tissue: WM and GM from DIR and T2W images were validated with the conventional 3D GRE-T1W images. Statistical analysis obtained in this study. The objective is to justify the benefit of the new techniques, which should reduce the tedious and time-consuming segmentation process but still provide the same result as in the conventional one.

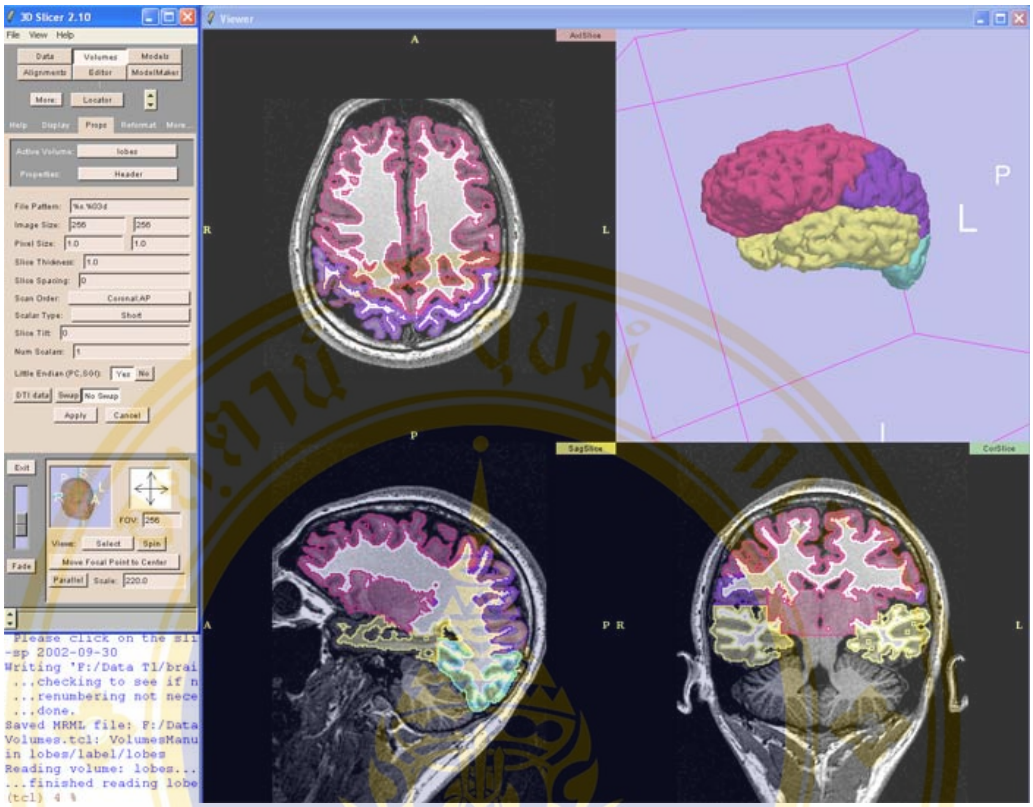


Figure 1.1 The 3D Slicer user interface has many controls over 3D and 2D scene. Segmentation results of brain lobes labeled in colors; Frontal lobe (red), parietal lobe (violet), occipital lobe (blue), and temporal lobe (yellow).

1.2 The objective of study

The aim of this study is to validate segmentation results from T2-weighted (T2W) and double inversion recovery (DIR) magnetic resonance images with the results from 3D gradient echo T1 weighted (3D GRE-T1W) images.

1.3 Benefits of study

Segmentation of gray and white matter on MRI is widely used in quantitative study of brain volumes change, especially in dementia studies. The combination of high contrast MR images can reduce the segmentation time.

1.4 Outline of the thesis

Chapter 1, Introduction, states the problem leading to this study, objective and benefit of study.

Chapter 2, Literature review, briefly describes about MRI, image segmentation, and relevant brain researches, respectively.

Chapter 3, Materials and methods, explains how to treats the segmentation of brain volume with healthy volunteers.

Chapter 4, Results, demonstrates brain volumes segmentation results, and statistical analysis is also included.

Chapter 5, Discussion, discusses about the usefulness and weak points of each segmentation method.

Chapter 6, Conclusion, presents final conclusion of the study and suggests on possible future work.

CHAPTER II

LITERATURE REVIEW

2.1 Basic Principles of MRI

There is hydrogen makes up about 80% of all atoms in the human body. The hydrogen nucleus has magnetic properties as called proton, which can be used in making MR images. The energy used in MRI is very low compared to X-ray and radioisotopes, which no harmful side-effects of this method have yet been identified. The magnets used are very large and form a tunnel in which the patient is positioned. The typical field strength used in the high field systems has been 1.0-3.0 testla (T).

MRI of the human body has superior soft-tissue contrast but is also a very complex and sophisticated method with a lot of new applications continuously being introduced. When put in the strong magnetic field all protons in the body are aligned parallel to the field. Slightly more than 50% of them are aligned along the magnetic field while the rest have an opposite direction. Because of this small "net magnetization" it is possible to measure the net magnetic vector. To produce images, different MRI sequences are used which contain a number of successive radiofrequency (RF) pulses together with different magnetic gradients.

The extraction is the initial RF pulse in the MRI sequence. When exposed to the RF pulse the net magnetic vector is flipped away from its original direction along the external magnetic field (B_0). The flip angle (FA) (often 90° or 180°) is proportional to the amount of energy applied. After excitation the RF pulse is switched off and magnetic vector returns to its original direction, thereby emitting energy in the form of a radio signal. This phenomenon is called relaxation and the time required differs according to the chemical and physical surrounding of each nucleus and is thus different in different tissues in the body. There are two major types of relaxation, T1 and T2, and images can be either T1-, T2- or proton density- (PD) weighted. The MRI sequence determines the repetition time (TR), i.e., the time between each excitation, and the echo time (TE),i.e., the time after which the emitted radio signal, the echo, is

collected. These parameters determine the image weighting (T1-,T2-,or PD-) which greatly influences the contrast in the final image. The magnetic field gradients are used to define the spatial encoding, slice thickness and orientation of the images and the final image is calculated by a Fourier transformation.

2.2 MR Pulse Sequences

Pulse sequences are the technique used for data collection known as the heart of MR measurements. They are computer program that control hardware of measurement process. Here, provided background of pulse sequences used in this study.

2.2.1 Conventional Spin Echo pulse sequence

The spin echo sequence is characterized by two user-selected time delays, TE and TR. The sequence consists of two radiofrequency pulses, the 90° pulse that creates the detectable magnetization, and the 180° pulse that refocus it at the TE and magnetic field gradient pulses Figure 2.

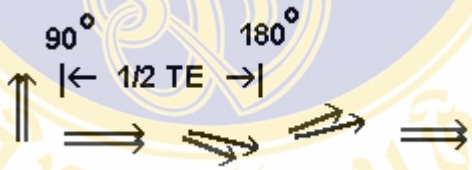


Figure 2.1 Spin echo magnetization diagram

In the SE situation the contrast between different tissues, in the final image, are determined by the TR and TE. The TR primarily determines the influence of the T1 relaxation in the image, and the TE determines the influence of T2 relaxation. In order to get T2-weighted image, the TE has to be chosen so as to get a large signal difference depending on T2 between different tissues. With short TE the differences are minimal while with longer TE they grow. At the same time the TR has to be long enough to minimize the influence of the T1 relaxation in the image. Similarly, the TE in a T1-weighted image has to be kept short in order to reduce the influence of T2-weighting. The typical T1-weighted SE sequence has a short TR and a short TE, and the typical T2-weighted sequence has a long TR and long TE.

2.2.2 Turbo Spin Echo pulse sequence

This is a spin echo technique for fast imaging based on the use of multiple spin echoes per excitation; each echo has a different preparation gradient encoding and all echoes are used for one imaging. A sample pulse sequence is shown in Figure 2.2. These TSE pulse sequence use multiple 180° RF pulse to produce up to 16 spin echoes within a single TR. Because of the difference between echo time in conventional SE and the effective echo time in TSE fat will have lost signal at long echo times. Both factors have to be taken into account when reading the images. As a result of increased incidental magnetization transfer effects, brain tissue will be darker, and CSF relatively brighter.

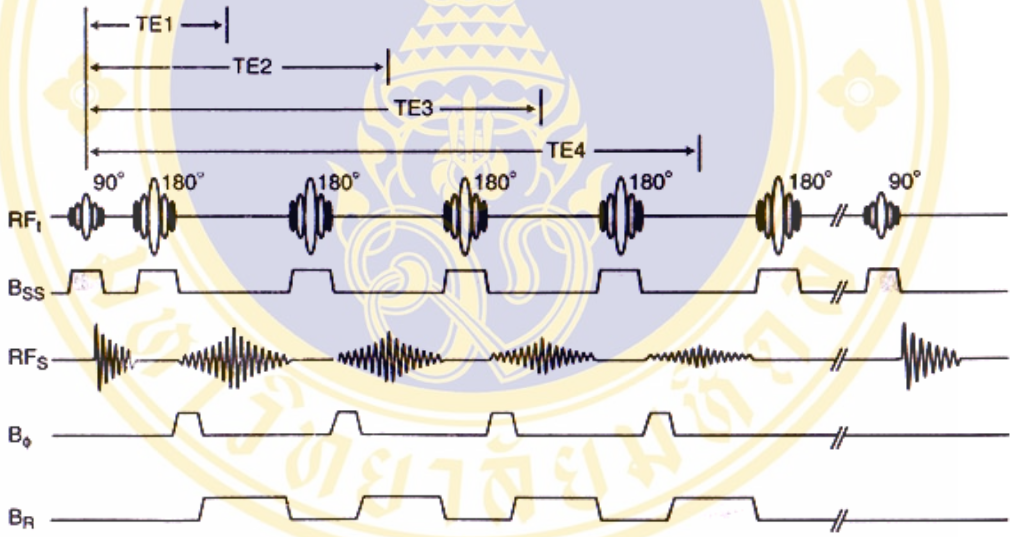


Figure 2.2 Turbo spin echo sequence (Bushong: 2003)

2.2.3 Gradient Echo pulse sequence

Gradient echo (GRE) pulse sequence is known as a major class of pulse sequences. When SE sequences use 180° RF pulse to refocus the transverse magnetization, gradient echo sequences are characterized by the lack of 180° refocusing RF pulse. And then, the echo signal is formed after a reversal of gradient pulses only (Figure 2.3).

In general, GRE sequences are significantly fast for obtaining T1-weighted, T2-weighted images. The speed of GRE sequences has made them the technique of

choice for obtaining T1-weighted images from a volume of tissue. GRE sequences are frequently used for T1-weighted three-dimensional (3D) volume that can be reformatted to display the slice in any plane in case of isotropic in voxels.

3D-GRE-MR image is a protocol to obtain images for the MR segmentation. However, the image is quite difficult for segmenting of gray and white matter region in the brain due to its low contrast between these two parts.

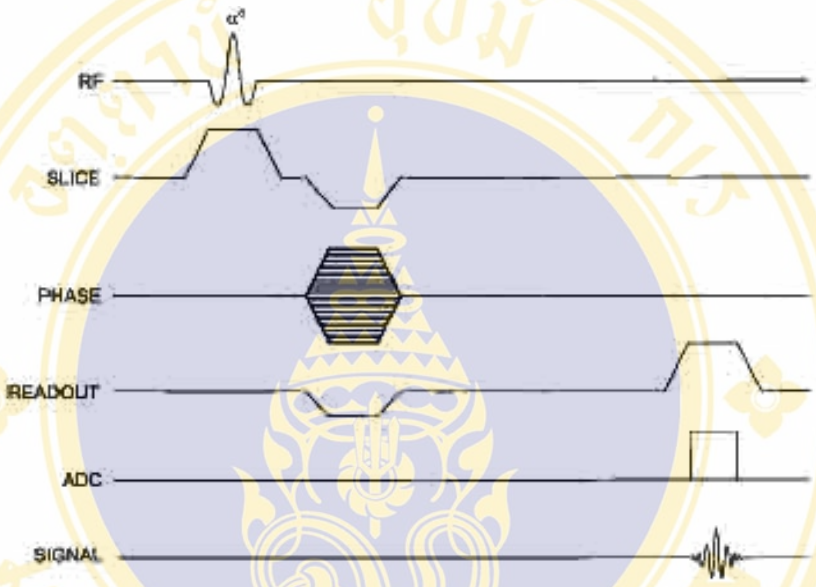


Figure 2.3 Gradient echo pulse sequence diagram. (Brown: 1999)

2.2.4 Inversion recovery pulse sequence

Inversion recovery (IR) sequences are typically derived from SE sequences. A 180° RF pulse is applied prior to the primary excitation pulse to invert the new magnetization (Figure 2.4). After this pulse, T1 relaxation occurs in which the net magnetization from each tissue passes from an inverted condition through zero net magnetization to a relaxed condition. The major application of inversion recovery sequences is for suppression of tissue. Selecting a TI when a tissue is at zero net magnetization will cause the tissue to generate no signal.

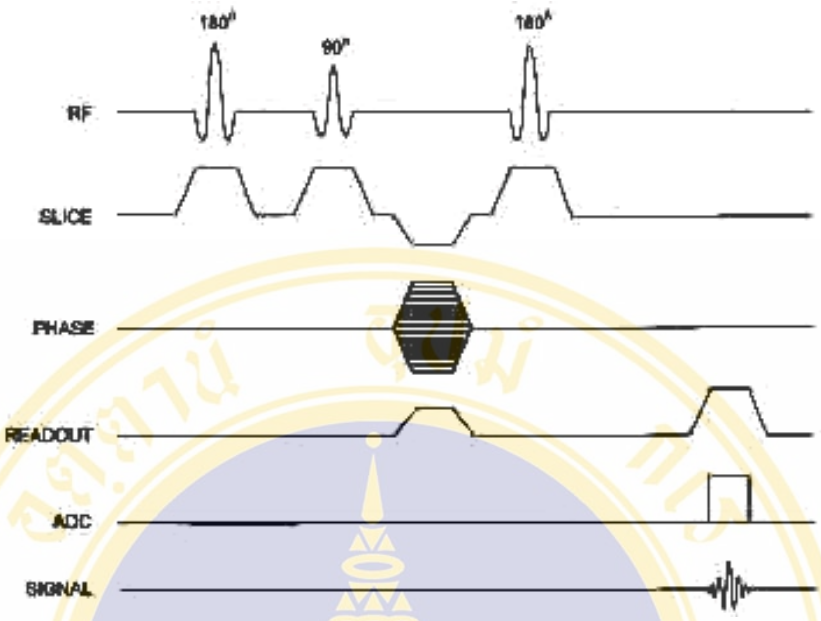


Figure 2.4 Inversion recovery pulse sequence timing diagram. (Brown: 1999)

2.2.5 Double inversion recovery pulse sequence

A double inversion recovery (DIR) sequence was designed to select gray or white brain matter image. Figure 2.4 showed conventional inversion recovery (IR) sequences that can be used to null the signal of a single tissue by choosing of the appropriate inversion interval TI. For the case where the z- magnetization is fully recovered this is:

$$TI = \ln 2 \cdot T1$$

where T1 is the tissue's longitudinal relaxation time.

Using an additional inversion pulse allows fat and fluid to be nulled simultaneously, and is termed a double inversion recovery (DIR) sequence. This works best if they have very different relaxation times. Figure 2.5 outlines a simple explanation of the DIR sequence applied to null cerebrospinal fluid (CSF) and white matter signals.

First, a 180° inversion pulse is applied without an associated imaging gradient, inverting magnetization throughout the imaged volume. Such an inversion pulse is referred to as a *nonselective inversion*. Next, a second inversion pulse is applied during application of slice-select gradient. This second pulse imparts an additional 180° rotation to the spins in the slice, returning magnetization to its equilibrium state.

Spins outside the slice, however, remain inverted. In the interval TI_1 between the inverting pulses, brain tissue magnetization recovers almost fully, while CSF, with its substantially longer T1, recovers to only a small fraction the equilibrium magnetization. The second inversion interval TI_2 is chosen to null white matter magnetization. Gray matter, with a longer T1, remains negative and generates a signal. CSF magnetization recovers slowly to pass through the null point at the same time as white matter. The structures of the brain are complex. Multiple folds can mean that gray matter and white matter, and CSF can lie within the same voxel. Methods of segmentation are based on image analysis of differences in intensity caused by differences in relaxation times and proton density between tissues. The DIR technique offers a method of segmenting the brain directly, without the need for image processing and ignores the problem of partial tissue volumes within the voxel. (Redpath TW and Smith FW: 1994)

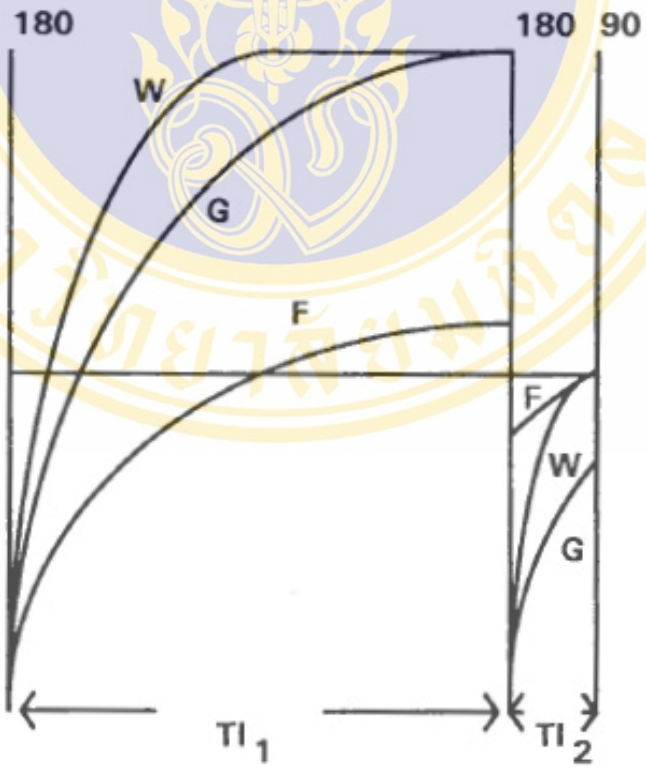


Figure 2.5 The evolution of Mz through the inverting intervals TI_1 and TI_2 is sketched for cerebrospinal fluid (F), gray (G) and white (W) matter.
(Redpath TW and Smith FW: 1994)

2.3 Brain MRI Techniques

Various considerations predominate when imaging the brain. For such an application, clear delineation of cerebrospinal fluid (CSF) is needed, as is the depiction of an altered T2 due to brain abnormalities. For imaging the brain, the volume of interest is roughly cubic, so a standard quadrature volume coil fitted to the head is often adequate, although phased-array technology can improve the signal-to-noise ratio (SNR).

For brain imaging, the only adipose tissue is in the scalp or bones or below the skull base so chemical shift techniques are not needed for routine imaging. The relative absence of fat in the brain also allows use of a low sampling bandwidth to increase the SNR

Standard T1-weighted spin echo and T2-weighted fast spin echo (FSE) images are generally used in multiple planes, supplemented by post-contrast T1-weighted images. Recently, additional techniques, such as fluid-attenuated inversion recovery, diffusion and perfusion techniques, magnetic resonance angiography (MRA), and proton spectroscopy, have become routine at many centers.

2.3.1 T1-weighted images

Most T1-weighted imaging of the brain utilizes the conventional spin echo technique, with the field of view (FOV) fitted to the body part. A matrix size of 256 x 256 pixels is standard. Although three-dimensional (3D) gradient echo techniques may be used to reduce the acquisition time, decrease the slice thickness, or both, image degradation at the skull base due to air-tissue interface is potential problem; such degradation can be reduced using the shortest possible TE.

Another alternative technique for obtaining T1-weighted contrast with minimal artifact at the skull base is FSE imaging with a short TR, short effective TE (TE_{ef}), and short echo train. These images are slightly blurred relative to standard spin echo images, but they can be obtained more rapidly, which allows dynamic contrast-enhanced imaging, such as for the pituitary gland. For most applications, however, the gradient echo technique is more efficient than the FSE method.

2.3.2 T2-weighted images

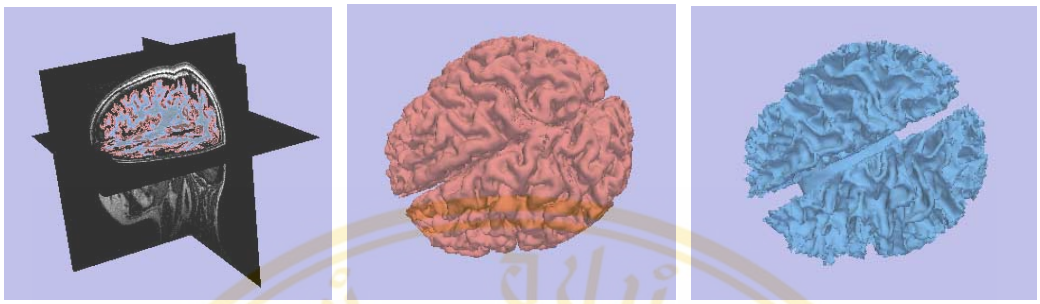
The conventional dual spin echo (SE) technique has been a standard component of protocols for imaging the brain and spine, but at most centers it has been replaced by the far more efficient FSE techniques. FSE imaging yields imaged with a high SNR, improved spatial resolution, and superior depiction of CSF spaces with shorter acquisitions. The rapid repetition of multiple refocusing radiofrequency (RF) pulse reduced motion artifacts due to CSF motion. The dual FSE technique can be used to generate intermediate-weighted images with a long TR and a short TE, such as for the spine, but these images are often omitted.

The abandonment of standard SE T2-weighted images is not universal, however. Advantages of standard SE include increased sensitivity to the susceptibility effects of hemorrhage and an improved dynamic range resulting from lower signal intensity from CSF compared with most T2-weighted FSE images. The imaged often have less blurring, and small subtle white matter lesions may be depicted with grater clarity. One option is to obtain two planes of T2-weighted imaging: one with FSE and one with SE.

For routine brain imaging, there is no need to suppress the signal from adipose tissue. For high-resolution imaging, the 3D steady-state free precession technique can yield thin slices with a high SNR and high contrast between fluid and tissue.

2.4 Image Segmentation

Image segmentation is the process of partitioning an image into region parts that are homogenous with respect to one or more characteristics or features, or isolating specific objects in an image**.** (Bankman: 2000) Image segmentation is important in medical applications, such as feature extract, shape analysis, image measurements, and image display. There is no one standard segmentation method that can be successfully used in all applications. Rather, a variety of segmentation techniques have been proposed, many of them are for specific proposed. There are three general types of segmentation approaches; manual, semiautomatic and automatic. Comparison of three segmentation types as shown in Table 2.1(Miller: 2002). An example of 3D medical image segmentation is illustrated in Figure 2.6



(a) (b) (c)

Figure 2.6 Example of 3D medical segmentation showing a) three orthogonal sections through a 3D MR image of the human head segmented into GM (red) and WM (blue); b) and c) the 3D model generated for GM and WM respectively.

Table 2.1 Comparison of segmentation techniques.

Techniques	Advantages	Disadvantages
Manual segmentation	- Simple - Results relate well to operator's perception	- Time consuming - Require an knowledge operator - Laborious - Operator bias - Low precision
Semiautomatic segmentation	- Faster than manual - Reproducibility	- Complex analysis methods - Limit application for specific region - Require operator input - Possible operator bias
Automatic segmentation	- Fast - Good reproducibility - Reduce operator input	- Complex analysis methods - Limit application for specific region - High precision - Error prone

2.4.1 Manual Segmentation

Manual segmentation involves interactive delineation of the structure boundary by operator. Many factors can affect the reproducibility of manual tracing. Room lighting, time of day, monitor brightness and contrast setting, operator fatigue or alertness, and other factors may have an effect on the accuracy of the border drawn. Even if these factors are eliminated, it is virtually impossible for the operator to repeat the exact same border around the structure. The disadvantages of this method are often time consuming, error prone, subjectively biased, and not reproducible. But manual segmentation is often the most accurate approach if an expert is doing the work and is not fatigued**.**

Multiple operators and images obtained from different scanner increase the variability of the defined borders. Manual segmentation may also be slow and tedious. Attempts to improve the manual segmentation task try to increase the speed and comfort of operator. Because this is no gold standard to judge segmentation, manual segmentation is used for comparison to an automatic technique (Fiez JA et al: 2000, Kaus MR et al: 2001).

2.4.2 Semiautomatic Segmentation

Semiautomatic segmentation is the process that is possibly the most practical and common form of segmentation. That is, a combination of computer image processing and manual intervention is used to segment and partition images. The computer attempts to automate much of the work. The user generally initializes the process with some boundary or starting information and then oversees the process and corrects erroneous results. The best of the semiautomatic methods are interactive and intuitive and have effective mechanisms for allowing the computer and human to work easily together.

2.4.3 Automatic Segmentation

Automatic segmentation is an algorithm attempts to segment and partition features and objects within an image without human intervention. Such an approach is often compute intensive and may be error. The ideal goal is that automatic techniques

would be accurate, reproducible and applicable to all images in order to relieve the labor of manual definition and editing.

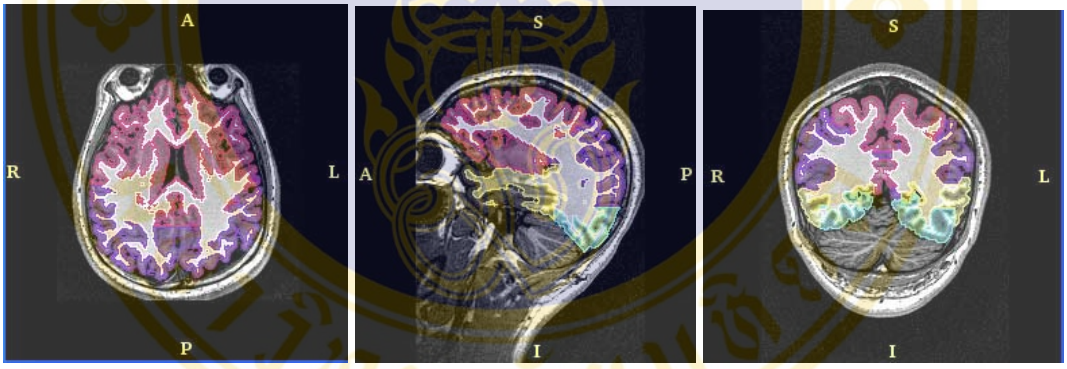
Hartmann et al (1999) measured and quantified difference of brain structures by using a fully automatic atlas-based method and validated with manually contour and repeated the measurements. Results showed that both methods are robust and accurate, even in atrophy by chronic alcoholic cases.

Furthermore, most segmentation techniques can be classified as region-based techniques that look for regions satisfying a given homogeneity criterion or boundary-based techniques that look for edges between regions with different characteristics. Most image segmentation methods use one image modality. Their performance can be enhanced by combining images of different modalities, such as multi-spectral segmentation (Reddick WE et al: 1997) or image acquired over time.

Among region-based segmentation methods, the most common ones are thresholding, clustering, region splitting and merging, and region growing. (Bankman: 2000) Thresholding is the simplest region-based segmentation method in this technique a threshold is selected and an image is divided into two groups of pixels: one having values less than the threshold and the other with the values greater or equal to the threshold. The threshold can be set globally for the entire image, or can be locally adjusted in an adaptive manner. In addition, methods have been proposed for automatic setting of an optimal threshold value (Gonzalez: 2000) Segmentation approaches based on Thresholding can produce acceptable results only in simple situations. Thresholding approach can be enhanced with mathematical morphology. (Gonzalez: 2000) Such algorithms, although usually simple, can provide effective and computationally efficient ways to segment complex medical structures. An example of the output of such an algorithm is illustrated in Figure 2.7

Clustering segmentation methods partition the image into clusters of pixels that have strong similarity in the feature space. Each pixel is examined and assigned to the cluster that best represents the value of its characteristics vector of feature of interest. Region splitting and merging is another region-based segmentation method. (Gonzalez: 2000) The image is subdivided initially into a set of arbitrary disjointed regions that are then merged and split in an attempt to satisfy certain conditions. Region growing starts from a set of “seed” points and assigns adjacent pixels or

regions to the same group if their image values are similar enough, according to some predefined criterion. (Bankman: 2000) A typical representation of region growing methods is watershed segmentation. The idea behind boundary-based segmentation methods is to extract object boundaries and to segment regions enclosed by the boundaries. (Bankman: 2000, and Gonzalez: 2000) These algorithms typically rely on an edge detector, such as Sobel, Prewitt, Roberts, or Canny. (Gonzalez: 2000) One of the most successful classes of boundary-based segmentation strategies are methods based on active boundaries. This line of work was inspired by the pioneer work on active contours that is the 2D version of the approach. The idea is that the object contours are modeled as deformable curves that automatically deform and attempt to align with image edges, at the same time preserving certain predefined properties such as smoothness, proximity to certain landmarks, sharp corner, etc.



(a) (b) (c)

Figure 2.7 Contour of the segmented brain lobes using thresholding and mathematical morphology are shown in a) axial, b) sagittal and c) coronal sections through the 3D GRE MR image of the head.

Often the complexity of medical structures requires the design of application specific segmentation methods that embody concepts from both region-based and boundary-based approached. For example, an algorithm for the segmentation of the cortex is described (Zeng et al: 1999) that, in addition to use image information, restricts the cortical thickness to be within a predefined range, which greatly improves its performance. A more general way to incorporate prior knowledge into segmentation algorithms is by statistical approaches. The idea is to segment a number of objects from a certain class, learn the statistics of the shape variability of each

object, and then use each to constrain the segmentation of a new object from the same class. Such an approach has been used to segment the corpus callosum from 3D MR images of the head. (Leventon: 2000)

2.5 Gray Matter and White Matter Measurements

Brain tissues can broadly be divided into white and gray matter volumes. The white matter is consisting of numerous myelinated axonal tracts, connects gray matter structures where concentrations of neuronal cell bodies are to be found, to each other and the rest of the nervous system. The spatial relationships between WM and GM and CSF are complex. Therefore, the measurements of the volumes of the brain WM and GM are varies considerably according to the choice of measurement method.

There are two main problems for brain segmentation. First, the brains are atrophic. In in-homogeneity of biological variations in different structures, there is more potential for partial volume effect between gray matter and CSF, and consequently voxels may be misclassified. The partial volume effect made the tissue boundary blurred. Missed segmentation can be reduced by using high resolution scans with small voxel size, especially isotropic 1 mm^3 (Good: 2002).

Second, the probably more important pathology may be associated with signal change and reduction in gray and white matter contrast. The intensities are sensitive the imaging parameters, there haven't been a clear correspondences between intensities and the biological tissue. Resulting in overlaps of the intensity ranges among different tissues (Juan He: 2000 and O'Donnell: 2001). GM and WM contrast is less sharp than brain-CSF contrast and is strongly dependent upon sequence parameters. For example, GM-WM contrast is inverted between T2W imaging and T1W imaging.

Harris (1994) demonstrated manual segmentation method for determination of the WM, GM, CSF volumes and method's reliability. The gray-white ratio was strongly correlated with the mean gray-white ratio setting, which is determined by the brightness of the displayed image. This related brightness artifact could be corrected by a suggested method, resulting in a valid and reliable method.

In MRI several types of volume estimation maybe used, but all are based on Cavalieri's principle that the volume of a structure is calculated by the area of the

structure on each slice multiplied by the slice thickness. This estimation of the true volume is only valid when all the slices are of equal thickness, the whole structure is measured and the first slice measured is positioned randomly. Jack et al (1990) showed that a technically experienced person with detailed knowledge of the relevant anatomy, using the tracing and thresholding technique, could reproduce volume measurements with a coefficient of variation (SD/Mean) within 2%. Interobserver variability was within the same range.

Different approaches to GM and WM measurements in MRI have been studied. For clinical use, the estimated values must be reliable and accurate when, unfortunately, many techniques fail on these criteria in an unrestricted clinical environment. (Salih QA, et al: 2005)

2.6 Validation techniques

Validation is the process of evaluating a new procedure to determine whether it satisfies specific requirements. Researcher in segmentation of MRI data has applied many techniques. But it is complicated due to no frame of reference or no gold standard to compare the methods. Results in many researches were validated only in visual or qualitative studies. Simulated data, phantom data manual segmentation are mostly used to assess segmentation accuracy. (Kapur T, et al:1996, Kikinis R, et al:1992,Zeng, et al:1998, Thacker and Jackson A:2001)

In this study, GRE pulse sequence images were used as input for reference methods. T2W and DIR images were proposed methods images. Volumes results of methods were compared by using statistical analysis.

CHAPTER III

MATERIALS AND METHODS

The overall materials and methods in this study were illustrated in the following flow chart. Each section details were described in respectively.

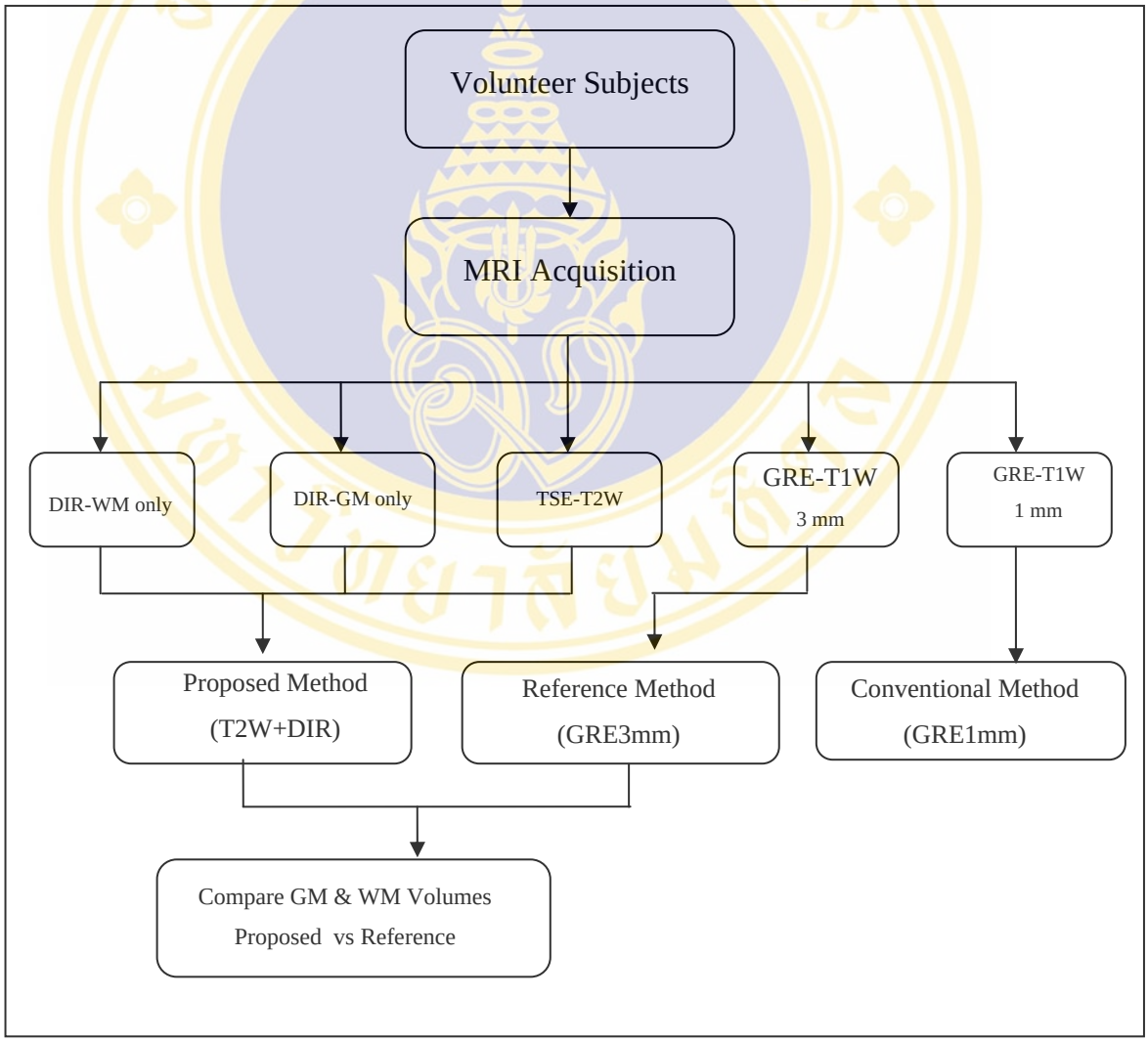


Figure 3.1 The flow chart summarize of overall project materials and methods.

3.1 Materials

In order to provide studies protocol, these materials used were described to specific in the research study and conventional one.

3.1.1 Volunteer Subjects

The healthy normal volunteers group was consisted of 5 men and 3 women, with an average age 28.5 ± 3.3 years (range 24 to 34). All volunteers were informed that MRI is without known hazard, with only a few exceptions. For examples, all electrical and magnetic equipments must be removed or not function properly, and should expect to be noisy and motionless during examination. Ethical consideration on MRI brain research could be found in Illes J, et al: 2004

3.1.2 MRI Acquisition

All MR images used were acquired on a Philips scanner 1.5 Tesla at Her Majesty's Cardiac Center, Faculty of Medicine Siriraj Hospital.

The image volumes cover brain cortex exclude cerebellum with 38 contiguous of 3.0 mm slice thickness with 256 x 256 pixels per slice, and an in-plane pixel size of 0.898438 mm images were acquired in 5 protocols: DIR-GM only, DIR-WM only, TSE-T2W, TSE-IR and GRE-T1W. In additional GRE-T1W was also acquired in 5 volunteers with 124 contiguous of 1.0 mm slice thickness and an in-plane pixel size of 1.0 mm images. The MRI scan parameters were presented in the table 3.1. GRE-T1W images were used as the standard reference for validation.

3.1.3 Data Transfer and Segmentation Software

Image dataset were acquired in DICOM format with header information. However, header information, such as patient’s details, was removed while image information was still remained.

The brain tissues volume segmentation techniques were implemented on the 3D Slicer version 2.1 downloaded from www.slicer.org, an open-source software package developed and maintained at the Surgical Planning Laboratory at Brigham and Women's Hospital, run on a personal computer (Pentium IV 2.4 GHz, RAM 1.5 GB, and NVIDIA Graphics card).

Table 3.1 MRI scanning parameters in this study.

Scan Protocol	Scan Parameter			Scan time (minutes)
	TR	TE	Flip	
DIR-GM only	12606	25	90	4.37
DIR-WM only	17616	25	90	6.27
TSE-T2W	3857	100	90	3.59
TSE-IR	3000	40	90	4.48
GRE-T1W 3mm	8.3	4.1	8	4.55
GRE-T1W 1mm	8.2	3.7	8	10.16

3.2 Methods

This study used the semiautomatic segmentation tools with different pulse sequence of MRI inputs. Segmentation of brain volumes in this thesis was divided into the proposed and conventional methods, in order to validate the new method with the conventional one. Segmentation steps of proposed and conventional methods were described respectively in the following sections.

3.2.1 Proposed Methods (T2W+DIR)

The proposed segmentation procedures were started from TSE-T2W image to select bright regions in image as CSF. The threshold was selected with a little over range for gap protection between outer parts of brain, or said, it was used as barrier layer.

Next, DIR-GM only image, GM region was selected by thresholding, attempted to cover all of GM. Try to fill the gap between GM that make the GM border in order to serve the further dilation of WM.

After that thresholding from DIR-WM only image, and got WM region which may not cover all part, however, WM was removed outer part and used in the next step.

As the regional segmentations were completed, then overlaid label maps into this sequence: CSF, GM, and WM. Next, followed by WM dilation filled up the gap between GM and WM. Moreover the cerebellum must be removed by drawing trace between the cerebellum and the cerebrum and around cerebellum that was comfortable by segmenting along the sagital direction. Resulting in the brain was divided into 3 volumes: GM, WM and CSF, with different colors. CSF was changed label into black for removing and left only WM and GM for volume measurements.

Moreover, 3D models were generated for better visualization in correction step. After the surface of label maps were corrected, the brain volume segmentation was done with measuring volume of GM and WM. Segmentation steps followed as diagram in Figure 3.2.

3.2.2 Reference Method (GRE3mm)

According to the fact that there was no gold standard for segmentation, conventional methods used GRE-T1W images that widely used in clinical brain researches. The different slice thickness utilized to compared with the proposed methods, and also examine the different within conventional methods.

GRE-T1W 3mm images were used as input for segmentation. This method was used as a reference to validate proposed method with the same slice thickness. The segmentation steps had a little different from proposed method. It used only one image sequence to segment both GM and WM volumes. Figure 3.3 demonstrated steps in these methods.

Reference method started from WM segmentation by thresholding, followed by removing outer part of WM. And then, another threshold selected GM with might have some tissue connections to scalp. After outer GM was removed, WM was overlaid to get the final label map, removed cerebellum to obtain brain volumes. The 3D model could be made for visualization some incorrectness may be seen and were corrected by manual tracing. Finally, the segmented brains were measured GM and WM volumes in ml.

3.2.3 Conventional Method (GRE1mm)

GRE-T1W 1mm images were used as input for this segmentation method. The conventional methods were used here to represent the real problem in clinical usages, and to compare the results with proposed method used in this study. The segmentation steps were the same as in reference method.

3.2.3 Time Measurement

Time measurement started after MRI data was imported to segmentation tool (3D Slicer) and stopped at the finished WM and GM labels. After that segmentation time was determined for the comparison between proposed and reference methods.

3.2.4 Statistical Analysis

To assess the validity of the proposed method, scans from 8 volunteer subjects were segmented by one investigator. But there were only 5 cases in GRE -1mm method. Due to a very small sample size, the statistics included these parameters: Mean, SD, CI, and paired t-test of brain volumes and segmentation time. Scatter plot of segmented volume from proposed and reference method by Pearson correlation was included.

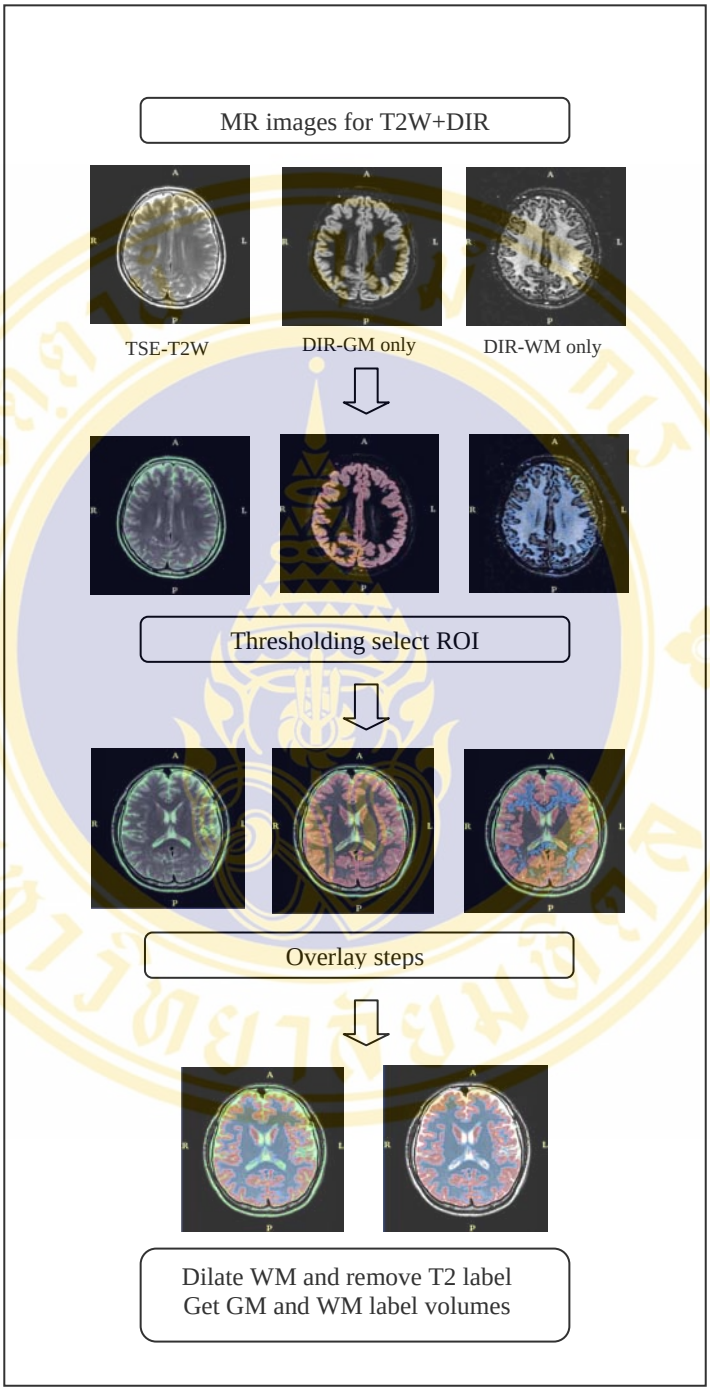


Figure 3.2 Proposed segmentation methods diagram.

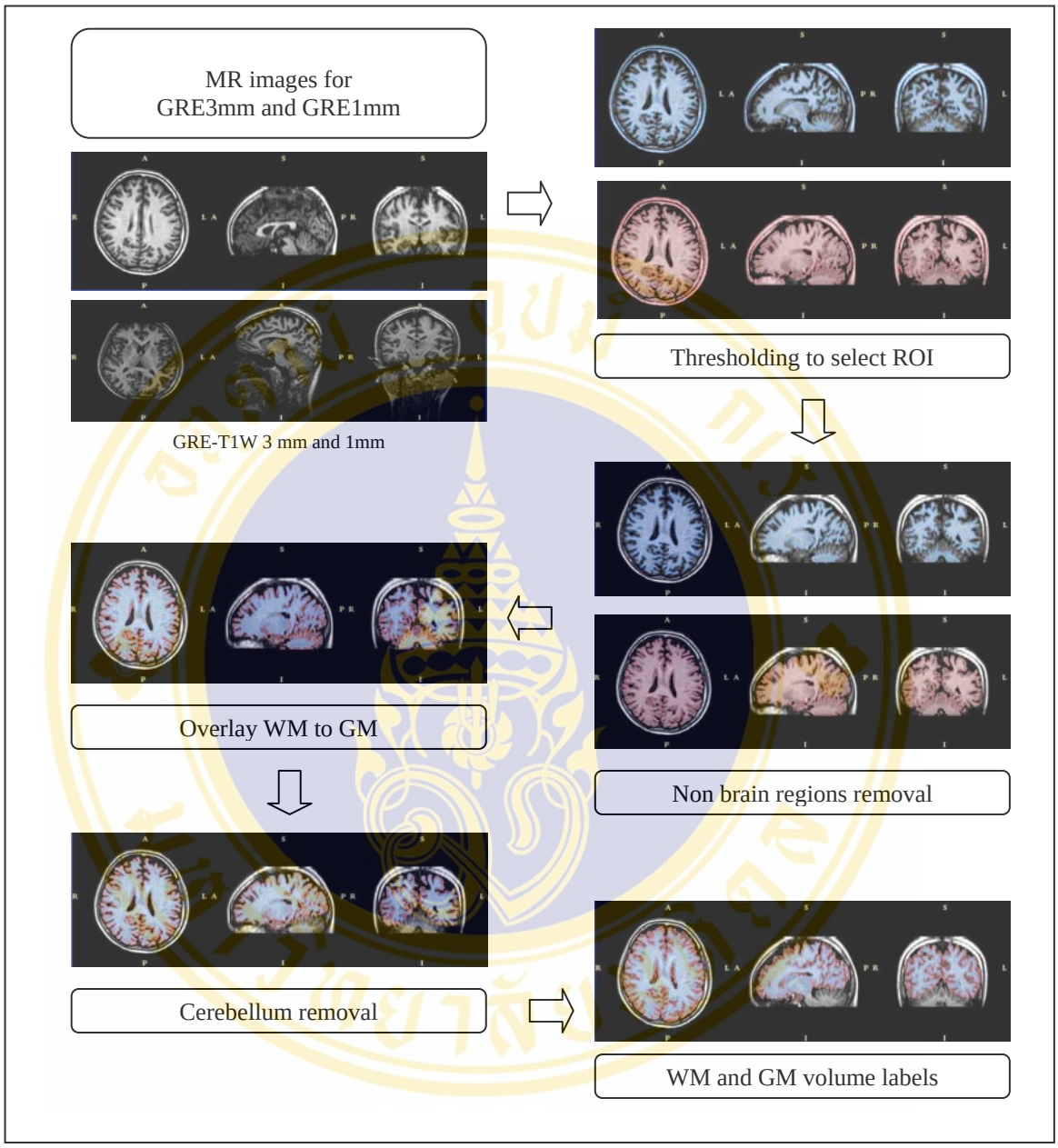


Figure 3.3 Reference and conventional segmentation methods diagram.

CHAPTER IV

RESULTS

MR brain volumes of eight healthy volunteers were segmented by 3 methods as described in section 3.2. In all cases, brain tissue selection based on observer anatomical knowledge judgment. The proposed method was validated in this study.

4.1 Comparison of segmented volumes from T2W+DIR and GRE-3mm

This study compared brain volumes segmented from 2 methods. Brain volumes were measured using GRE1mm, which is tedious and labor intensive, use in conventional method because of appropriate scan time, and compared with using multiple sequences, T2W+DIR, to provide high tissue contrast with prolong scan time.

Data were acquired from eight healthy volunteers who participated in this study. Image acquisition of brain excluded cerebellum and transfer to segment by 3D Slicer. Figure 4.1 is a scatter plot of brain volumes from T2W+DIR versus GRE3mm.

The two methods of WM segment are clearly associated: Pearson Correlation = 0.7799. Whereas the two methods of GM segment are not clearly associated: Pearson Correlation = -0.3985. The diagonal line in Figure 4.1 is the line of equality: the two methods are in perfect agreement only if all measurements lie along this line. It can be seen that more of the points lie above the line than below it, suggesting that WM segmented volumes from T2W+DIR tends to be higher than segmented from GRE3mm.

The extent of agreement could be examined by plotting the differences between the pairs of measurements on the vertical axis, against the mean of each pair on the horizontal axis. Such a plot is shown in Figure 4.2. The mean difference of WM volume between segmented from T2W+DIR and segmented from GRE3mm was 57.81 ml. There was thus a clear tendency for WM volume to over segment in T2W+DIR, by an average of 57.81 ml. This is shown by the dashed horizontal lines in Figure 4.2.

The dotted horizontal line in Figure 4.2 and 4.3 corresponds to the 95% limits of agreement, given by the mean difference plus or minus twice the standard deviation of the differences. The approximately 95% of differences in WM and GM are normally distributed lie within this range from -23.23 ml to 138.85 ml and -137.74 to 145.12 ml, respectively. The mean difference and the 95% limits of agreement were calculated to decide whether the methods are sufficiently in agreement for one to be used in place of the other.

The measured volumes results obviously presented that case of WM volume as larger in volume difference, however, in the same case GM as less in volume difference. Visualization of the results showed significant differences between T2W+DIR and GRE3mm. The brain volumes visualization of this case will emphasize this issue, as illustrated in Figure 4.4 In contrast, there were some case with have close WM while larger in GM, show in Figure 4.5 and 4.6

The comparison of proposed method, reference method and conventional method in term of confident interval of WM and GM segmented volumes were presented in Figure 4.7 and 4.8.

4.2 Segmentation time

Segmentation time was recorded to compare among techniques used in study. The average time of each method varied according to the variability if brain anatomy in subject. Figure 4.9 showed the segmentation time in GRE1mm was 183.38 ± 4.7 minutes, reduced to 56.13 ± 5.6 minutes in GRE3mm, and in T2W+DIR was 16.38 ± 2.2 minutes.

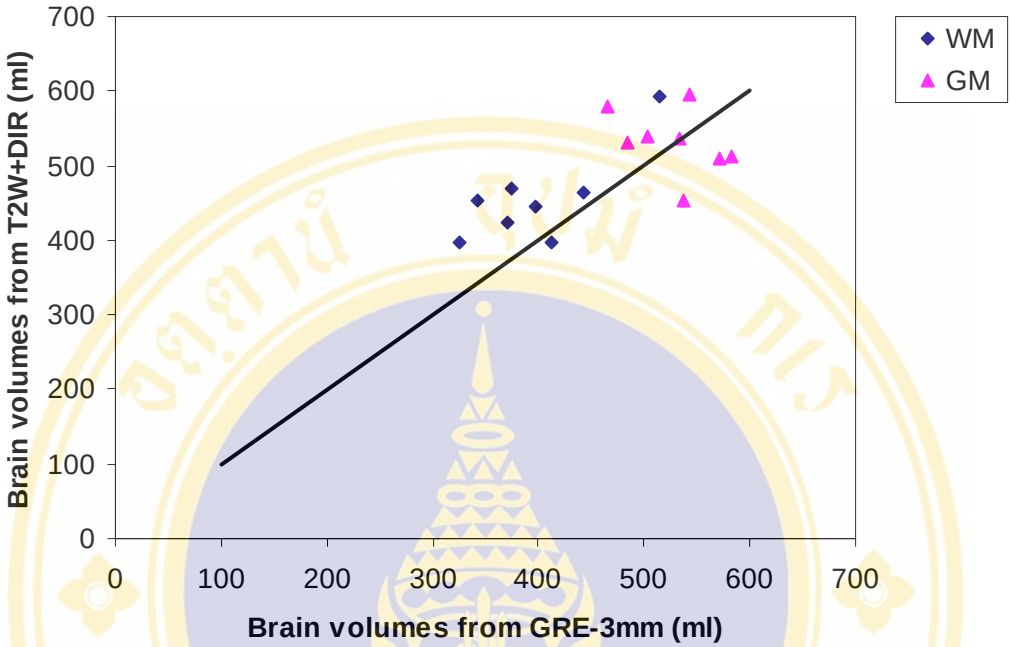


Figure 4.1 Scatter plot of brain volumes segmented fromT2W+DIR versus segmented from GRE3mm in 8 healthy volunteers. The solid line is the line of equality.

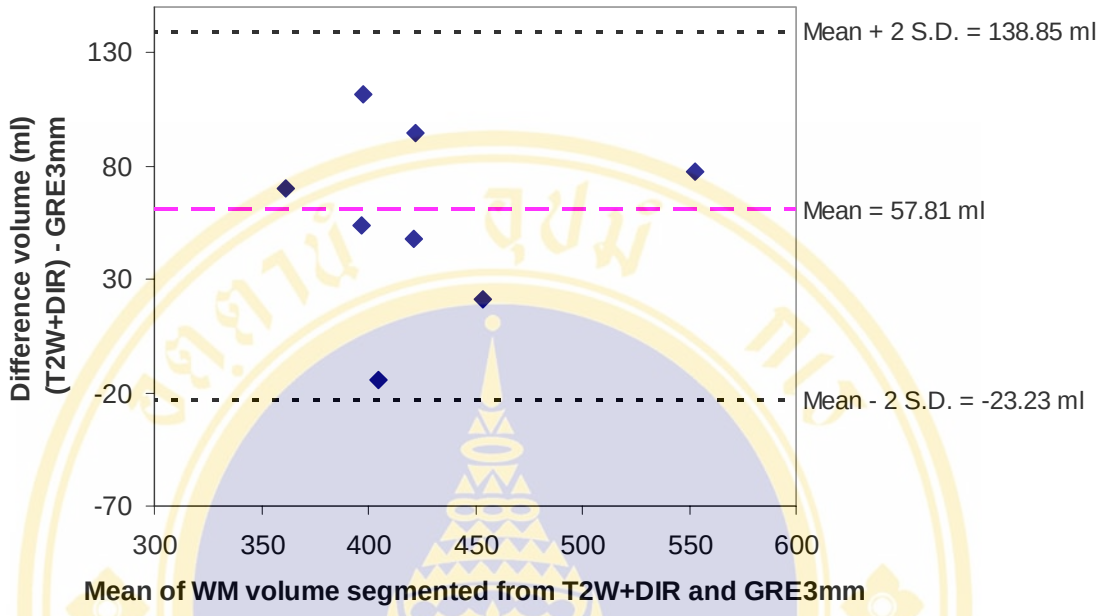


Figure 4.2 Scatter plot of WM volume segmented from T2W+DIR minus segmented from GRE3mm (vertical axis) against mean of WM volume segmented from T2W+DIR and GRE3mm (horizontal axis) in eight volunteers who participated in this study. The dashed horizontal line corresponds to the mean difference (57.81 ml) while the dotted horizontal lines correspond to the 95% limits of agreement.

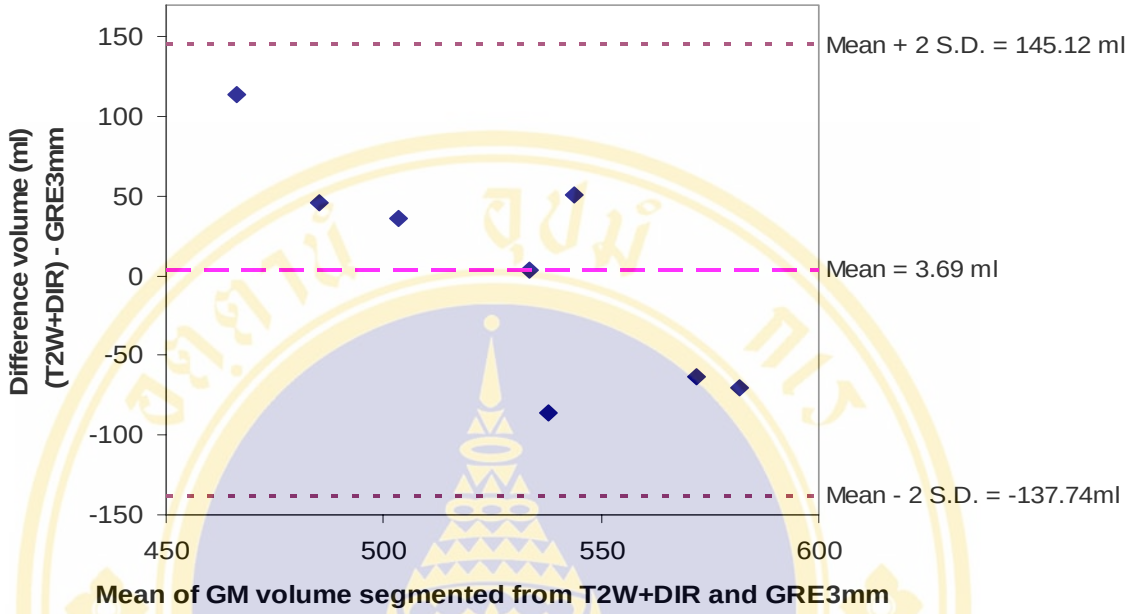


Figure 4.3 Scatter plot of GM volume segmented from T2W+DIR minus segmented from GRE3mm (vertical axis) against mean of WM volume segmented from T2W+DIR and GRE3mm (horizontal axis) in eight volunteers who participated in this study. The dashed horizontal line corresponds to the mean difference (3.69 ml) while the dotted horizontal lines correspond to the 95% limits of agreement.

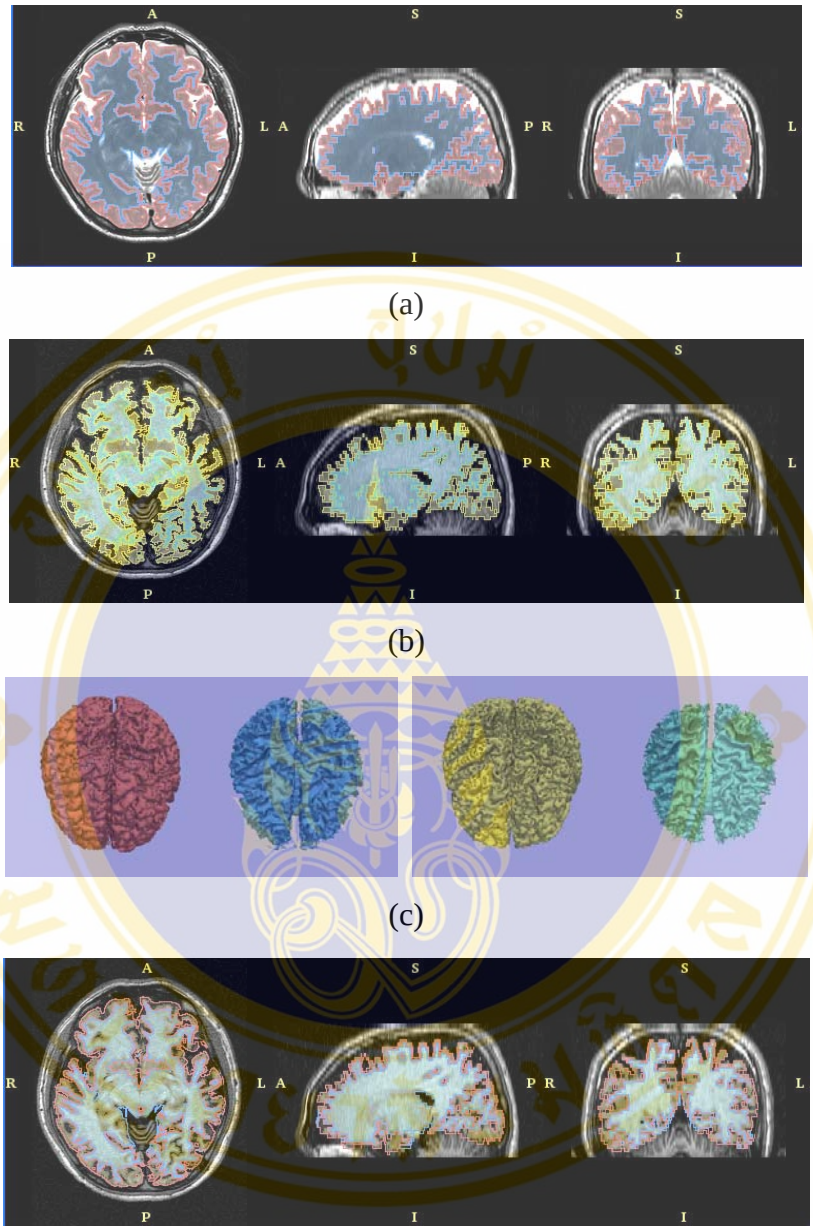
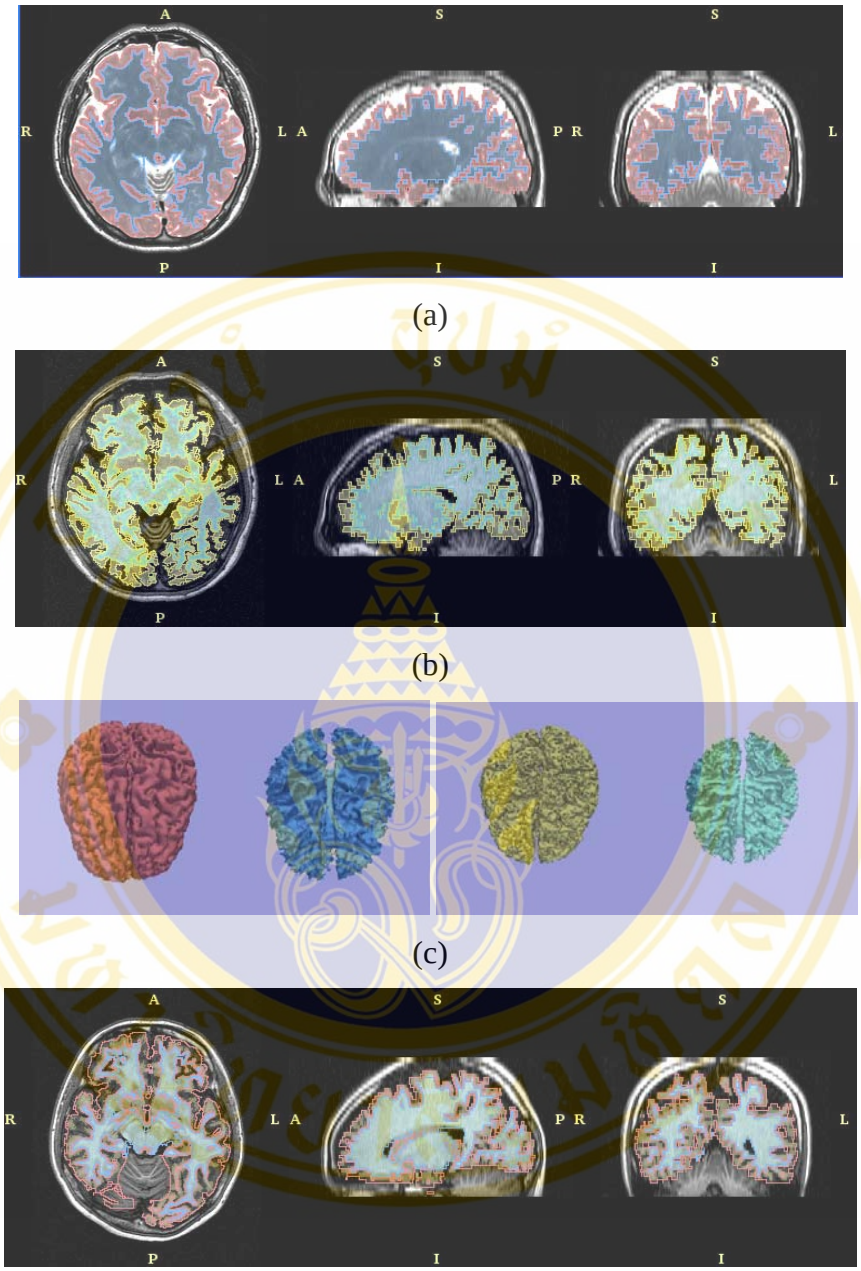


Figure 4.4 WM and GM segmentation results Case 2 from proposed method, (T2W+DIR) was compared with reference method (GRE3mm). a) T2W+DIR; WM is blue, GM is red, b) GRE3mm; WM is green, GM is yellow, c) Left; model generated from T2W+DIR, Right, model generated from GRE3mm, and d) Label from T2W+DIR overlay with GRE3mm into T1W background.



(a)

(b)

(c)

(d)

Figure 4.5 WM and GM segmentation results Case 4 from proposed method, (T2W+DIR) was compared with reference method (GRE3mm). a) T2W+DIR; WM is blue, GM is red, b) GRE3mm; WM is green, GM is yellow, c) Left; model generated from T2W+DIR, Right, model generated from GRE3mm, and d) Label from T2W+DIR overlay with GRE3mm into T1W background.

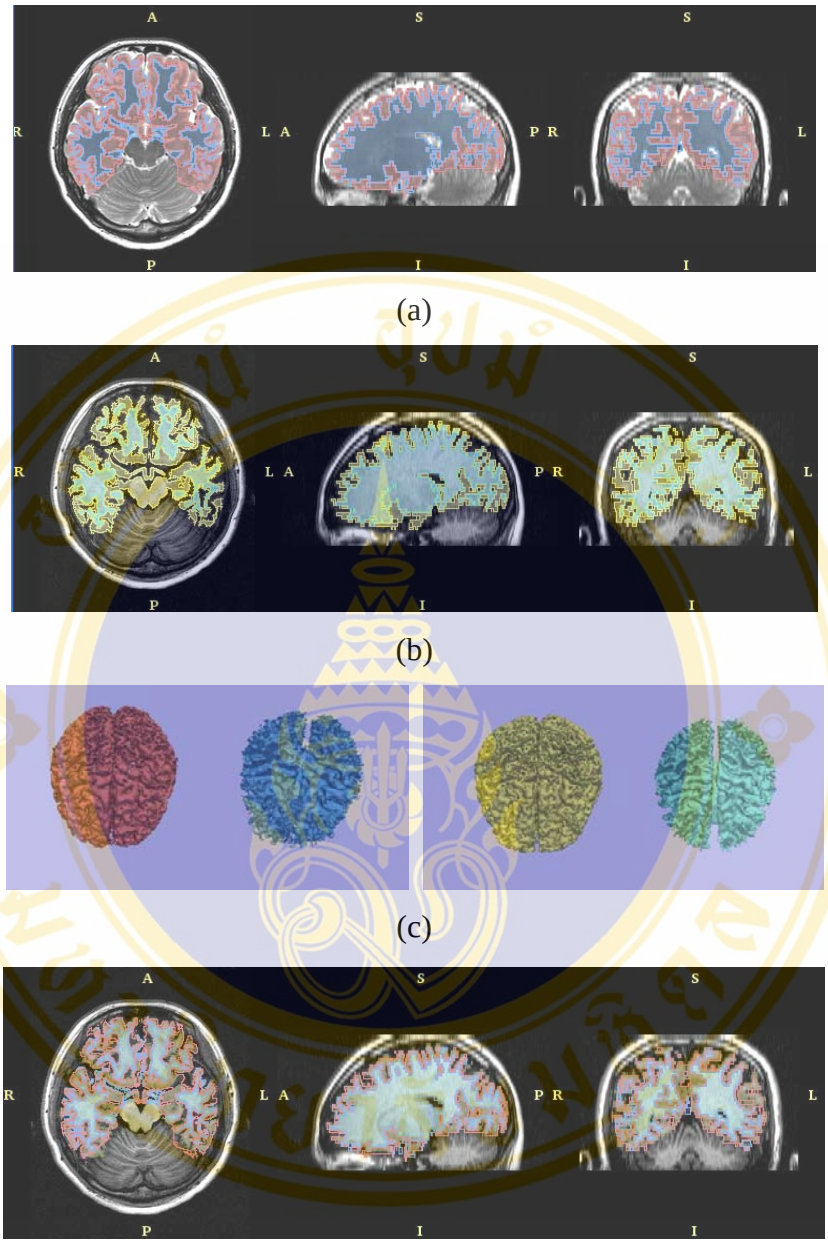


Figure 4.6 WM and GM segmentation results Case 5 from proposed method, (T2W+DIR) was compared with reference method (GRE3mm). a) T2W+DIR; WM is blue, GM is red, b) GRE3mm; WM is green, GM is yellow, c) Left; model generated from T2W+DIR, Right, model generated from GRE3mm, and d) Label from T2W+DIR overlay with GRE3mm into T1W background.

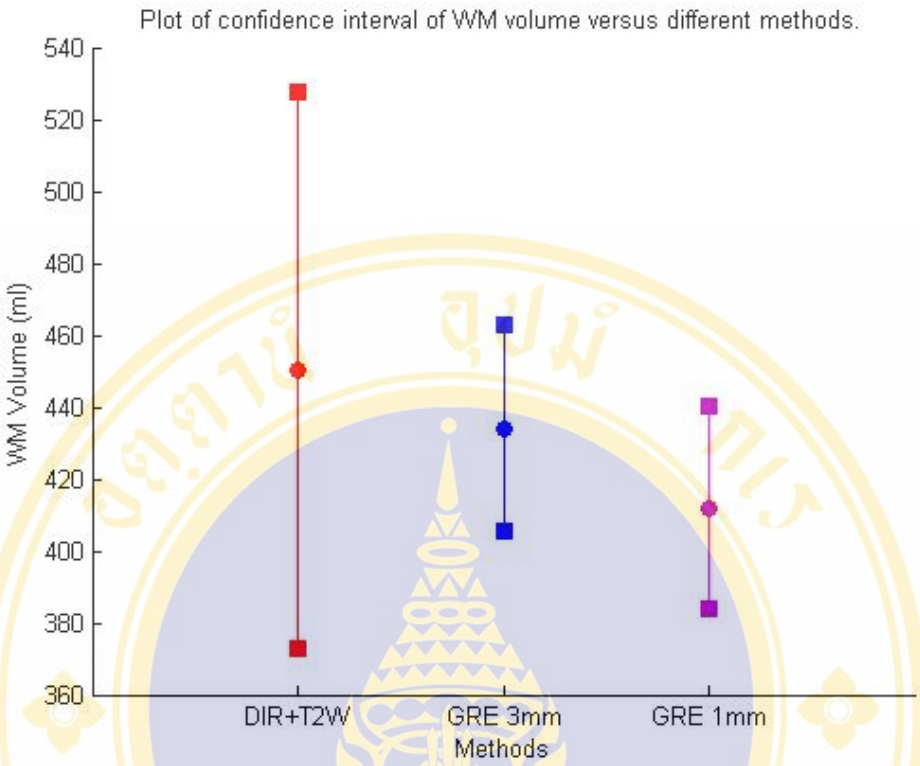


Figure 4.7 Comparison plot of segmented white matter versus different methods

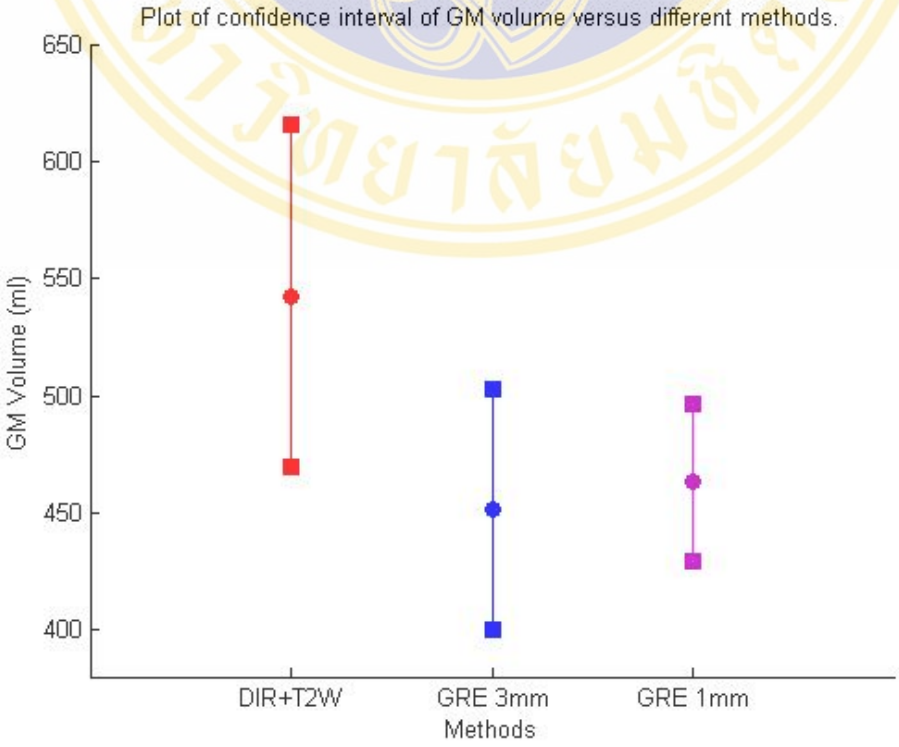


Figure 4.8 Comparison plot of segmented gray matter versus different methods

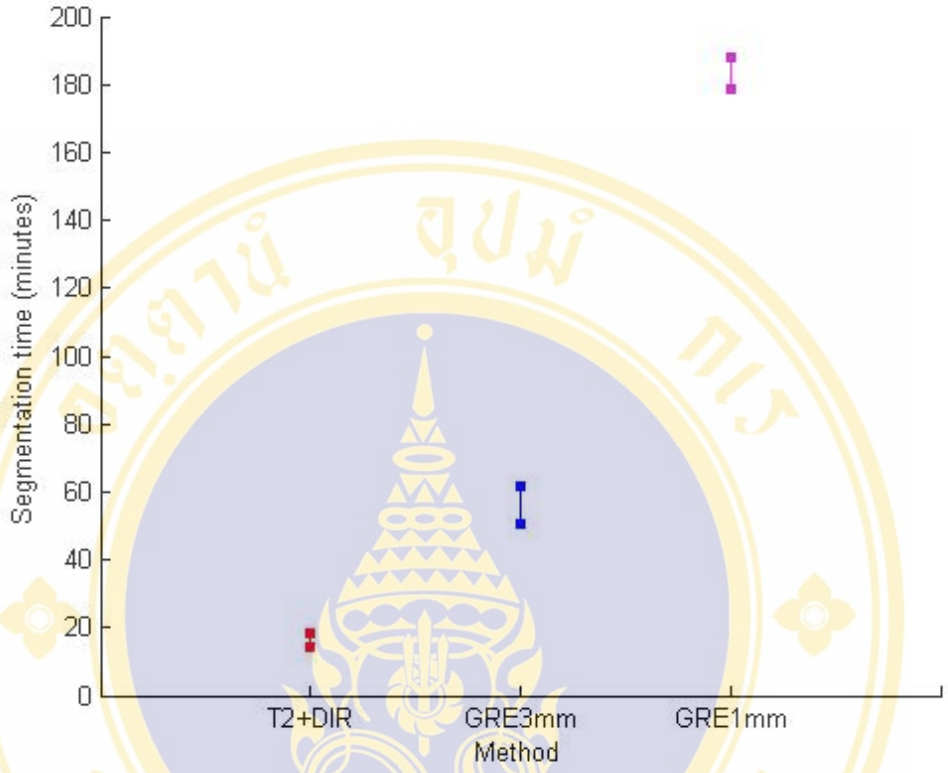


Figure 4.9 Plot of segmentation time in different method.

CHAPTER V

DISCUSSION

The recently available MR pulse sequences were improved segmentation tasks by providing high contrast between tissue regions. A combination of MRI techniques is also helpful in order to increase in histological specificity.

In this chapter provided the discussion of brain segmented results, comparing with other works, limitation of our method, and suggestion.

5.1 Brain Volumes Segmentation Study

The present study was designed to validate our proposed method (T2W+DIR) with reference (GRE3mm) and conventional (GRE1mm) methods. The 3 interested cases were selected from segmented data in this study to represent the advantages and disadvantages of our proposed method.

As can be seen in Figure 4.4 (d) the segmented result of case 2 presented that the contour of each method closely in display by merging label maps into the GRE image. But in quantity, the result showed that only GM of this case was closed to result from reference method, except in WM resulting in largest different in volume result. In contrast, case 4 in Figure 4.5 results in over GM contouring with minimum of WM different between methods. Even seen the closed in quantity of brain volume, but not all label map slices were the same in the different method result. From case 5 showed almost both WM and GM segmented from proposed and reference method was the same, however, Figure 4.6 (d) showed that there was some missed area in WM region from proposed method appeared in reference method.

From above results, the segmented of WM and GM from proposed and reference method were valid if correct the region by using manual segmentation of both tissues or using volume visualization to help at this step.

The statistical analysis showed in Figure 4.7 and 4.8, the wide range of CI in WM and GM caused by error of some cases that have over estimated segment in threshold selection step.

The results from this study had been segmented according to observer judgment that required anatomical knowledge and segmentation skills. The error could cause by either method or observer judgment. However, this factor could be corrected by using manually segmented by experienced radiologist whose labels were use as ground truth to compare results as in Yu S (2002).

5.1.1 Advantages of the proposed method

The proposed method is faster than conventional method. And get a result closed to the conventional method, especially in WM tissue.

According to there was no gold standard to compare segmentation results, however we can use the conventional method with adjudged of pulse sequence to get the closed to proposed method for comparison.

The proposed method can be used at initial step for quantitative research of brain volumes measurements such as in dementia studies that necessary to measure brain volume periodically.

5.1.2 Disadvantages of the proposed method

When using morphological operations will result in over or missing region, after used this method have to correct some area with manual tracing.

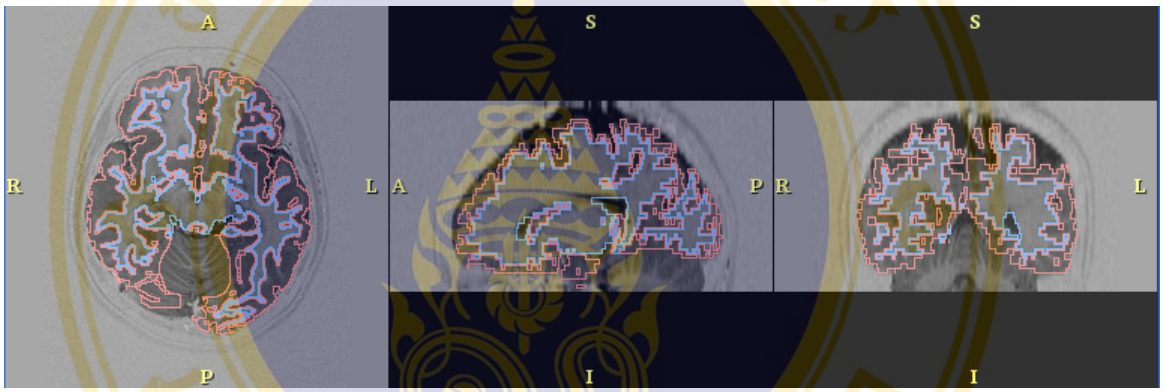
There was lack of accuracy and reliability test in this study, which required experienced rater and larger in sample sizes.

5.2 Segmentation time

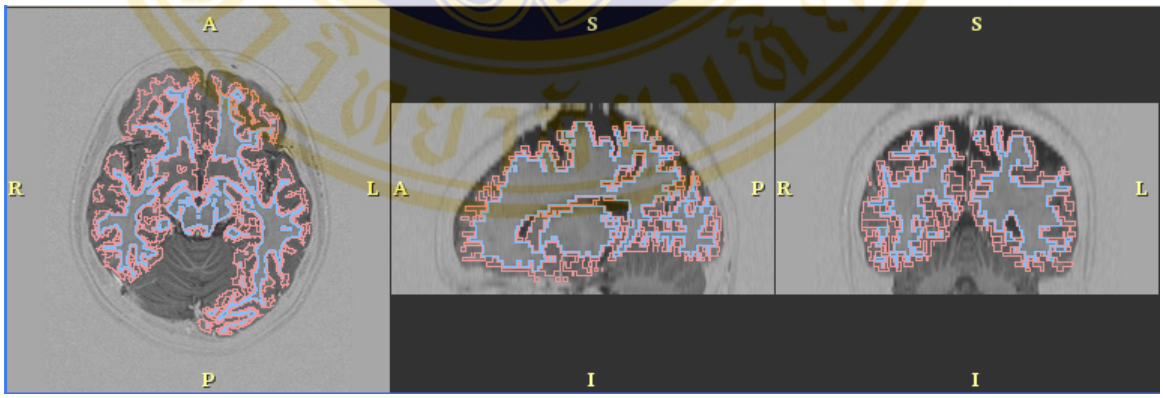
From Figure 4.9 demonstrated that the proposed method reduced more than 50 percent of reference segmentation time. Because the method used the high resolution image, reduce manual tracing operation and use dilation method to fill up the gap between tissues.

5.3 Limitations of our method

For better visualization of brain contour, we used IR sequence to compare segmented results from proposed and reference method. As illustrated in Figure 5.1, in proposed method segmented from T2W+DIR obviously presented reasonable segmented contour compare with a reference method segmented from GRE-3mm that showed the lower of GM and WM region. However, in proposed method can see that some area was over tissue border also, from this figure (a) in axial plane, the region of WM is over but less than in figure (b).



(a)



(b)

Figure 5.1 Comparison of GM and WM contour segmented from (a) proposed method (T2W+DIR) and (b) reference method (GRE3mm), overlay with IR images.

According to the input image for segmentation, the results were presented not the same as seen in segmented slide (Figure 4.3-4.5), due to the difference of image contrast leaded to misclassify some area with need high resolution to distinguish. Especially, in GM region segmented with GRE images, the unclear border of GM could not tell the correct anatomy masking, so the observer could not justify the actual point. However, the result can be justified more with manual tracing, but when merge into different type of image data, the label map could be not actually the same, will look better.

To segment with proposed method, the things should have exclamations are;

- Be careful with morphological operations, erosion and dilation results caused the over or under estimated region in some area, even correctly seen in segmented slice, but it can appear in other plane with a little point.
- Should look the brain anatomy only one plane when segmenting brain tissues, this study look in axial plane; the rest of planes use for justify and correct some area after visualization in 3D model.

5.4 Suggestions

For further studies, the alteration of pulse sequence such as reducing slice thickness into 1.5 mm or added the IR sequence to help visualization after finish segmentation procedure and to correct or remove the misclassification regions.

Moreover, accuracy and reliability of proposed method should be considered by experienced rater, repeat operations by observer that can be either inter-observer study or intra-observer study.

The sensitivity and specificity of proposed methods are also interested parameters that used for validation in the suitable of sample sizes. In case of this study might use the sample size more than 30 cases.

CHAPTER VI

CONCLUSION

Various segmentation methods have been presented, manual segmentation was the selected method used in this brain volume studies. According to the high contrast between brain tissues of image input which can reduce segmentation time, and provided such better images input. Proposed method combines thresholding and morphological operations to segment brain tissues. White and gray matter segmented volumes from proposed and reference methods were compared. The results demonstrated statistical significant with 95% confidence intervals.

In conclusion, the segmented results for WM of brain volume from proposed methods were not been found statistical difference from conventional methods. However, in GM need to justify the border of tissue, and carefully use of morphological operations, because the results will not validate with reference or conventional method. Whenever, the brain volumes label maps were obviously correct in anatomy landmark, the result between methods will not significantly difference. The segmentation time of proposed method reduced from reference and conventional method more than 50 percent. As a result, these proposed methods compensate segmentation time with a longer image acquisition time. The image acquisition must be optimized depending on specific proposed.

Possible Further Studies

1. The segmented results could be compared in term of pixel difference and the similarity index, especially in the most percentage difference case. This can show the reliability of this study.

2. The more sample sizes ($n \geq 30$) required to optimum the statistic requirement.

3. Use different pulse sequence or the same pulse sequence as this study with different in slice thinness, such as reduce to 1.5 mm. To get the more resolution, present clearly marking especially in GM border.

4. The image intensity and brightness should be controlled in segmentation steps.

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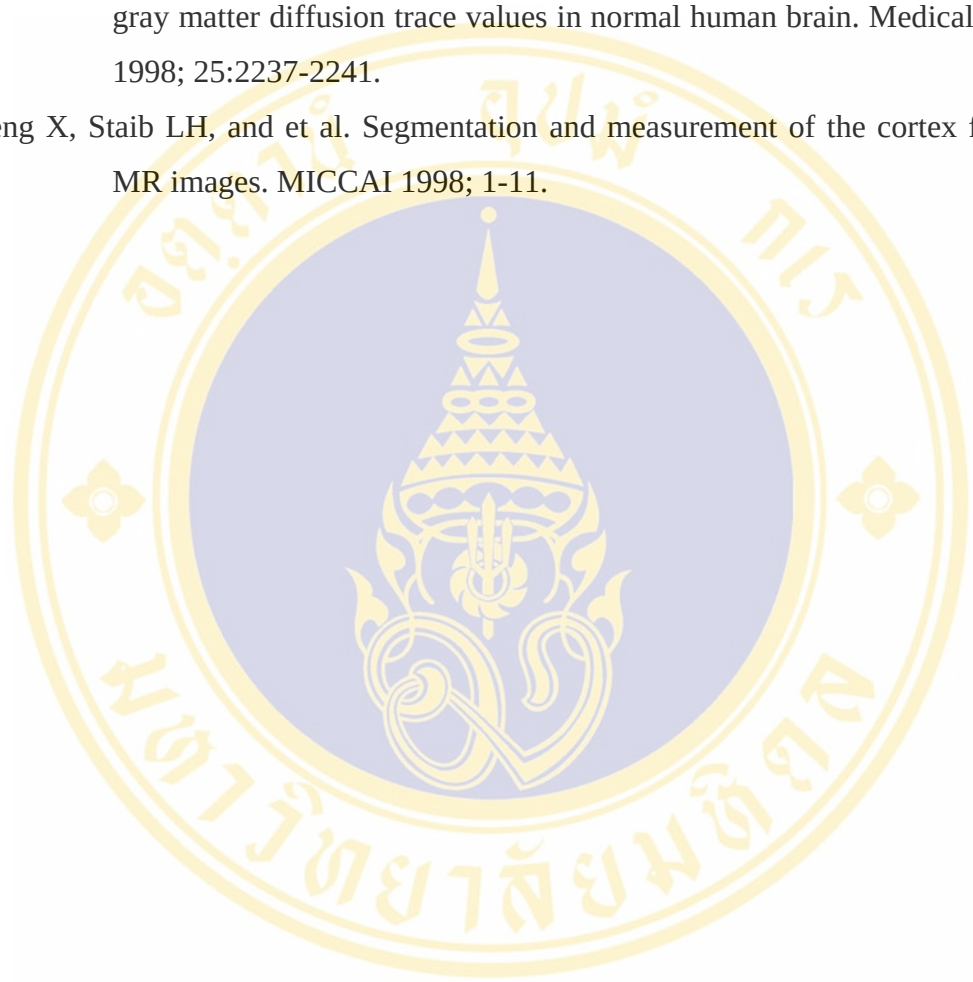

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