UNIVERSITI PUTRA MALAYSIA

EVALUATION OF 25 MIDLINE CEREBRAL STRUCTURES OF INFANTS BY THREE DIMENSIONAL ULTRASOUND AT A PUBLIC HOSPITAL IN MALAYSIA

NORHAFIDZAH BINTI MOHAMED SHARIF

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By

NORHAFIDZAH BINTI MOHAMED SHARIF

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Chair: Norafida Bahari, PhD
Faculty: Medicine and Health Sciences

Three-dimensional ultrasound (3DUS) examination was available in clinical setting for more than 20 years but 3DUS examination remained underutilized and not widely used in clinical practice. Routinely, in infant brain imaging, following two-dimensional ultrasound (2DUS) examination, Magnetic Resonance Imaging (MRI) examination would be performed for further evaluation of brain pathology if it was indicated. MRI examination had several limitations. 3DUS technique was developed to improve the existing of 2DUS technique. 3DUS had potential to be used broadly in clinical practice. Thus, dependency on MRI examination can be reduced.

This study was conducted to determine the potential of 3DUS scanning in evaluating the 25 midline cerebral structures of infant.

A total of 20 subjects with mean age of 9.40 ± 5.43 months participated in this study. The subjects underwent 2DUS and 3DUS examination after completed the MRI examination. The images of 25 midline cerebral structures obtained by MRI, 3DUS and 2DUS examination were evaluated by two (2) raters. The data was analyzed using Chi-square test, Cohen’s Kappa test, Intra-class Correlation Coefficient (ICC), Wilcoxon Signed Rank test, Passing-Bablok Regression and Bland Altman Analysis.

The raters evaluated most of the midline cerebral structures as excellent in MRI examination as compared to good visualization on 3DUS and non-visualization of image visualization in 2DUS examination respectively. There was no significance difference in disease diagnosis evaluated by raters in MRI examination. The visualization rate was moderate, fair and slight agreement with K < 0.36 at 95% CI and the overall agreement was 20% in 3DUS examination. The ICC was between 0.61 and 0.97 at 95% CI demonstrated good and very good agreement in 3DUS examination. There was no significance difference and no significance bias at 95% CI in measurement of the most of the midline cerebral structures between 3DUS and the both examinations demonstrated that 3DUS was interchangeable and acceptable technique. 3DUS was a reliable technique and can be used as alternative technique for MRI and 2DUS examination. The mean scanning times for 3DUS and 2DUS examination was 5.62 ± 1.92 minutes and 7.07 ± 1.74 minutes respectively, demonstrated that 3DUS was slightly faster than 2DUS examination.

3DUS examination was a reliable, feasible and reproducible technique in measuring the 25 midline cerebral structures. 3DUS examination can be used in clinical setting as alternative examination to MRI and 2DUS examination.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Sarjana Sains

PENILAIAN 25 STRUKTUR SEREBRUM TENGAH BAYI OLEH ULTRABUNYI TIGA DIMENSI DI SEBUAH HOSPITAL AWAM DI MALAYSIA

Oleh

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Pemeriksaan *Three Dimensional Ultrasound* (3DUS) telah berada dalam amalan klinikal selama lebih daripada 20 tahun tetapi pemeriksaan 3DUS masih kurang dimanfaatkan dan tidak digunakan secara meluas dalam amalan klinikal. Secara rutin, dalam pengimejan otak bayi, selepas peperiksaan *Two Dimensional Ultrasound* (2DUS), pemeriksaan *Magnetic Resonance Imaging* (MRI) akan didahului untuk penilaian selanjutnya jika diperlukan. Pemeriksaan MRI mempunyai beberapa batasan. Teknik 3DUS telah dibangunkan untuk memperbaiki teknik 2DUS sedia ada. 3DUS mempunyai potensi untuk digunakan secara meluas dalam amalan klinikal. Oleh itu, pergantungan pada pemeriksaan MRI dapat dikurangkan.

Kajian ini telah dijalankan untuk menilai potensi pengimbasan 3DUS untuk menggambarkan dan mengukur 25 struktur-struktur tengah serebrum bayi.

Sejumlah 20 subjek dengan min umur 9.40 ± 5.43 bulan telah mengambil bahagian dalam kajian ini. Subjek menjalani pemeriksaan 2DUS dan 3DUS selepas selesai pemeriksaan MRI. Imej 25 struktur-struktur tengah serebrum bayi yang diperolehi daripada pemeriksaan MRI, 3DUS dan 2DUS dinilai oleh dua (2) penilai. Data dianalisis menggunakan ujian Chi-square, ujian Cohen Kappa, *Intraclass Correlation Coefficient* (ICC), ujian Wilcoxon Signed Rank, Regresi Passing-Bablok dan Analisis Bland Altman.

Dalam pemeriksaan MRI, penilai menilai kebanyakan struktur serebrum tengah bayi sebagai cemerlang. Visualisasi imej pemeriksaan 3DUS dan 2DUS masing-masing menunjukkan visualisasi yang baik dan tidak visualisasi. Dalam pemeriksaan MRI, tiada perbezaan yang signifikan dalam mendiagnosis penyakit. Persetujuan kadar visualisasi adalah sederhana, kurang dan sedikit dengan K < 0.36 pada 95% selang keyakinan dan kesepakatan keseluruhan adalah 20% dalam peperiksaan 3DUS. ICC adalah antara 0.61 dan 0.97 pada 95% selang keyakinan menunjukkan persetujuan yang baik dan sangat baik dalam pemeriksaan 3DUS. Tidak terdapat perbezaan yang signifikan dan tiada berat sebelah yang signifikan pada 95% selang keyakinan dalam pengukuran kebanyakan struktur serebrum tengah antara 3DUS dan kedua-dua pemeriksaan menunjukkan bahawa 3DUS adalah teknik yang boleh ditukar ganti dan diterima. 3DUS adalah teknik yang boleh dipercayai dan boleh digunakan sebagai teknik alternatif kepada pemeriksaan MRI dan 2DUS. Min tempoh pengimbasan untuk pemeriksaan 3DUS dan 2DUS masing-masing adalah 5.62 ± 1.92 minit dan 7.07 ± 1.74 minit, menunjukkan bahawa 3DUS adalah lebih cepat daripada pemeriksaan 2DUS.

Pemeriksaan 3DUS adalah teknik yang boleh dipercayai, boleh dilaksanakan dan boleh diulang dalam mengukur 25 struktur serebrum tengah. Pemeriksaan 3DUS boleh digunakan dalam amalan klinikal sebagai pemeriksaan alternatif kepada pemeriksaan MRI dan 2DUS.

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I certify that a Thesis Examination Committee has met on 11 September 2017 to conduct the final examination of Norhafidzah binti Mohamed Sharif on her thesis entitled "Evaluation of 25 Midline Cerebral Structures of Infants by Three Dimensional Ultrasound at a Public Hospital in Malaysia" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Master of Science.

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LIST OF ABBREVIATIONS

RT VI	Right ventricle index
LT VI	Left ventricle index
RT TOD	Right thalamo-occiptal distance
LT TOD	Left thalamo-occiptal distance
RT AHW	Right anterior horn width
LT AHW	Right anterior horn widh
TVW	Third ventricle width
FVW	Fourth ventricle width
CCL	Corpus callosum length
GenuW	Genu width
BodyW	Body width
SpleniumW	Splenium width
GenuH	Genu height
CVH	Cerebral vermis height
CVW	Cerebral vermis width
TCD	Transverse cerebral distance
CMH	Cisterna magna height
PonsW	Pons width
RT BGW	Right basal ganglia width
LT BGW	Left basal ganglia width
RT CHW	Right caudate head width
LT CHW	Left caudate head width
IHFW	Inter hemispheric fissure width
ECSW	Extra cerebral space width
CDCG	Cortical depth of cingulate gyrus
2DUS	Two dimensional ultrasound
3DUS	Three dimensional ultrasound
AF	anterior fontanel
CT	Computed Tomography
DICOM	Digital Imaging and Communications in Medicine
ICC	Intra-class Correlation Coefficient
MF	mastoid fontanel
MP	Multi-planar
MRI	Magnetic Resonance Imaging
PACS	Picture Archiving and Communication System
SNR	Signal Noise Ratio
TGC	Time gain compensation
TUI	Tomographic ultrasound imaging
VCI	Volume contrast imaging

LIST OF ABBREVIATIONS

cm	centimeter
kg	kilogram
mg/kg	milligram per kilogram
MHz	megahertz
mins	minutes
mm	millimeter
n	sample size
P	level of significance
r	correlation coefficient
r^2	coefficient of determination
SD	standard deviation
T	Tesla

CHAPTER 1

INTRODUCTION

1.1 Research Background

In clinical setting, Magnetic Resonance Imaging (MRI) and ultrasound scanning were used to produce images of human body, purposely for disease diagnosis. Due to their advantage as non-ionizing radiation modalities, MRI and ultrasound scanning were recommended for infant imaging. MRI scanning became a preferred modality because ability to provide superior diagnostic information. Ultrasound scanning that was used before was two-dimensional ultrasound (2DUS) and ultrasound scanning was always the initial radiological examination as it was easily available.3DUS scanning was one of the advanced techniques in ultrasound technology but, unfortunately, it was not broadly used in radiological examination compared to in obstetric field. 2DUS scanning was a conventional method but it was widely used for several decades until now because the availability in clinical setting and the technician are more familiar with it. However, the 2DUS scanning was frequently upgraded with the latest technology in order to acquire optimum ultrasound images.

Ultrasound imaging became the first choice imaging examination for infant due to availability, user-friendly and can be used for bedside scanning. The infant who was diagnosed or suspected with any abnormalities by ultrasound examination would be evaluated further by using either Computed Tomography (CT) scan or MRI examination. However, in CT scan, radiation was involved. On the other hand, the infant with non-compatible MRI foreign body was contraindicated for MRI examination.

MRI scanning was not easily available and it was also an expensive procedure. MRI examination also take a long duration. Thus, the infant should be kept in same position throughout MRI examination in order to obtain good image quality. Routinely, single or multiple sedations was needed. Some of infant were required general anesthesia due to poor response to sedations. Hence, close monitoring by the anesthetic team was required until the infant was fully awake. If the infant failed to be sedated, the examination would be re-scheduled.

On the other hand, for ultrasound examination, there was no special setup of equipment was needed and no sedation required, therefore there was no involvement of other clinical team. The cost of ultrasound examination was much cheaper than MRI examination. There were many ultrasound units available in a hospital. So it was easier to schedule for ultrasound examination compared to MRI examination. There was continuous advancement in ultrasound technology introduced more features and provided useful diagnostic information.

American Institute of Ultrasound in Medicine (AIUM) underlined the excessive temperature as known risk factors can contribute to the biological effect. According to (Fowlkes, 2011), there were no significance adverse biological effects were observed for the temperature between 35 to 39˚C and duration of heating was up to 50 hours. According to Benacerraf, Shipp, & Bromley, 2006; Junewick, Martin, & Woolpert, 2007; Romero et al., 2014, 2DUS and 3DUS examinations were performed in less than 20 minutes and less than 2 minutes, respectively. To our knowledge, there were no absolute ethical issues as 2DUS and 3DUS examinations were conducted within the limit (body temperature is 37˚C and the duration of scanning took about 10 to 20 minutes).

Study on 3DUS technology was still ongoing to broaden the potentials and capabilities of this technique. The comparison study between 2DUS, 3DUS and/or MRI of the neonatal brain disease, found that ultrasound examination able to define the certain diagnosis but MRI examination failed to determine it in few cases (Epelman et al., 2010; Leijser, Steggerda, et al., 2009; Petropoulou et al., 2012). Most of the infant who underwent the diagnostic imaging scanning associated with the investigation of brain disorders. Commonly the brain disorders involved midline area consisted of the lateral ventricle, third ventricle, fourth ventricle, corpus callosum, cerebellum, cisterna magna, pons, basal ganglia, caudate nucleus, inter-hemispheric fissure, extra-cerebral space and cortical depth of cingulate gyrus.

1.2 Problem Statement

In infant brain imaging, ultrasound was the initial radiological examination for evaluation of intracranial pathology. Routinely, after 2DUS examination, MRI examination would be preceded for further evaluation if indicated. 3DUS scanning had limited availability in our country including equipment, experiences and experts. MRI examination had several limitations.

MRI scanning was not easily available and it was also an expensive procedure. MRI scanning was a longer procedure. Thus, the infant should be kept in same position throughout MRI examination in order to obtain good image quality.

Routinely, single or multiple sedations was needed. Some of infant were required general anesthesia due to poor response to sedations. Hence, close monitoring by the anesthetic team was required until the infant was fully awake. If the infant failed to be sedated, the infant would be given a new appointment date. Sometimes, there was contrast medium reaction occurred, thus further patient management was required. Only MRI-safe suit and the patient who was free from MRI-unsafe materials are allowed to enter the MRI room. There was limited size of coil thus the radiographer required to fit the small size of the infant's head with available coil in order to produce a good image resolution.

On the other hand, ultrasound scanning was broadly available in clinical setting. Ultrasound scanning was friendly user, quick examination and no sedation required. The price for ultrasound scanning was obviously cheaper than MRI examination. In addition the conventional 2DUS scanning technique was always updated with new technology. 3DUS scanning technique was introduced after 2DUS technique and already available in clinical setting for more than 20 years. However, the 3DUS scanning remained underutilized and only few examiners applied 3DUS in their clinical practice. We believed that the advanced technology in 3DUS scanning can provide adequate image resolution for disease diagnosis.

1.3 Significance of Study

The study of potential and capabilities of 3DUS on infant brain was conducted to provide awareness among healthcare providers such as clinicians, sonographers and radiologists to perform or request the 3DUS scanning. Therefore the dependency on MRI examination can be reduced.

1.4 Objectives

General Objective:

Assessing the potentials and capabilities of 3DUS examination in visualizing and measuring the 25 midline cerebral structures of the infant brain.

Specific Objectives:

This study was conducted to:

1) Compare the visualization of 25 midline cerebral structures of infant obtained by MRI, 3DUS and 2DUS examination.
2) Determine the measurement difference between two examinations consisted of MRI and 3DUS examination, MRI and 2DUS examination and 3DUS and 2DUS examination in measuring the 25 midline cerebral structures of infant.
3) Quantify the difference in scanning time for 3DUS and 2DUS examination of infant brain.
4) Identify the difference in size between left and right sides of infant midline cerebral structures obtained by MRI, 3DUS and 2DUS examination.
5) Identify the difference between male and female in measuring the 25 midline cerebral structures obtained by MRI, 3DUS and 2DUS examination.

1.5 Hypothesis

There was significance difference among the three (3) examinations. MRI examination provided superior diagnostic quality in evaluating 25 midline cerebral structures of infant brain followed by 3DUS and 2DUS examination. 3DUS examination of infant brain was a comparable technique with MRI examination of infant brain.

1.6 Expected Outcome

Based on the study design that has been conducted, we assumed that 3DUS is comparable to MRI in visualization and measuring the multiple midline cerebral structures. We were expecting also that the 3DUS is better than 2DUS in visualizing and measuring the multiple midline cerebral structures.

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