UNIVERSITI PUTRA MALAYSIA

POSTMORTEM COMPUTED TOMOGRAPHY AND POSTMORTEM COMPUTED TOMOGRAPHY ANGIOGRAM IN SUDDEN NATURAL DEATH

SAIFUL NIZAM BIN ABDUL RASHID

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By

SAIFUL NIZAM BIN ABDUL RASHID

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Doctor of Philosophy

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Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Doctor of Philosophy

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September 2020

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Introduction Post-mortem computed tomography (PMCT) acts as an adjunct to autopsy but with limitations in vascular and organs diagnosis. This is alleviated using postmortem computed tomography angiogram (PMCTA). Current PMCTA approaches and protocols are not based on Asian population. Whole-body PMCTA uses femoral approach while selective PMCTA uses neck approach. Whole body PMCTA using neck approach is more feasible in our mortuary. Sudden natural death is the commonest cause of natural death (COD) in Malaysia. A modified whole-body PMCTA scanning and infusion protocol based on body weight for the Asian population using the neck approach was derived and tested.

Methodology A prospective, double-blinded, cross over randomized control trial study was conducted. Each subject underwent PMCT, PMCTA and finally autopsy. Water-soluble contrast media combined with Polyethylene Glycol 200 was used. The reliability of the modified protocol in terms of diagnostic value for organ and vascular pathology in comparison to autopsy, diagnosing and comparing the COD as well as complications were documented. The confidence level (CL) in formulating the COD, PMCTA helps in the final COD compared to PMCT and decision on autopsy based on PMCT/PMCTA findings were assessed.

Results and Discussion 60 cases recruited with 46 males and 14 females (22-75 of age, mean of 45.6). 32 Malaysian and 28 non-Malaysian with Asian ethnicities, majority were Muslim. The *"embalming effect"* due to excessive amount of contrast media, higher infusion rate and pressure using the recommended protocol was documented at the initial stage of the study. This was eliminated by decreasing the amount of CM based on body weight and gradually increasing the rate and pressure during infusion. The whole body was analyzed based on anatomical systems and PMCT/PMCTA findings were

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comparable to autopsy. Similarity coefficient (SC) value of 0.876 for all 3660 variables analyzed and statistically significant showed a strong correlation. The vascular system has the strongest correlation. The commonest COD was cardiovascular death. 78.3% matched, 15.0 % minor and 6.67% major COD discrepancies between radiologists and pathologists. Strong relationship for both radiologists (SC :0.867 to 0.883) but slightly lower when compared to pathologists (SC value: 0.767). Hypothesis testing revealed significant results and concluded that there is relationship or similarity conclusion on COD between radiologists and pathologists. Radiologists CL was generally lower compared to pathologists. Highest CL was in diagnosing vascular pathologies. PMCTA increased their CL and helped in their COD compared to PMCT alone. Majority still needs full or limited autopsy.

Conclusion The new modified PMCTA protocol for the Asian population using the neck approach has been proven scientifically and statistically with high diagnostic value and promising results. Radiologists COD based on PMCT/PMCTA was comparable to autopsy especially in vascular-related pathology. The role of Forensic Imaging in Malaysia stays as an adjunct to autopsy and not to completely replace it with high potential for limited autopsy in the future.

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Pengenalan Tomography computed post-mortem (PMCT) bertindak sebagai tambahan untuk bedah siasat tetapi dengan batasan diagnosis vaskular dan organ. Ini dikurangkan dengan menggunakan angiogram tomografi terkomputeran postmortem (PMCTA). Pendekatan dan protokol PMCTA semasa tidak berdasarkan populasi Asia. PMCTA seluruh badan menggunakan pendekatan femoral dan PMCTA selektif menggunakan pendekatan leher. PMCTA seluruh badan menggunakan pendekatan leher lebih sesuai untuk bilik mayat kami. Kematian semula jadi secara tiba-tiba adalah penyebab kematian semula jadi *@ cause of death (COD)* yang paling banyak di Malaysia. Protokol imbasan dan infusi PMCTA seluruh badan yang diubahsuai berdasarkan berat badan untuk populasi Asia menggunakan pendekatan leher diperoleh dan diuji.

Metodologi Satu kajian percubaan kawalan prospektif, *double blinded*, cross over dilakukan secara rawak. Setiap subjek menjalani PMCT, PMCTA dan akhirnya autopsi. Media kontras larut air yang digabungkan dengan *Polyethylene Glycol 200* telah digunakan. Kebolehpercayaan protokol yang diubah dari segi nilai diagnostik untuk patologi organ dan vaskular dibandingkan dengan autopsi, mendiagnosis dan membandingkan COD serta komplikasi didokumentasikan. Tahap keyakinan *@ confident level (CL)* dalam merumuskan COD, PMCTA membantu dalam COD akhir berbanding PMCT dan keputusan autopsi berdasarkan penemuan PMCT / PMCTA dinilai.

Keputusan dan perbincangan 60 kes direkrut dengan 46 lelaki dan 14 wanita (umur 22-75, min 45.6). 32 orang Malaysia dan 28 bukan warganegara Malaysia dengan etnik Asia, majoriti adalah beragama Islam. "Kesan pembalsuan *@ "Embalming effect* " kerana jumlah media kontras yang berlebihan, kadar infusi dan tekanan yang lebih tinggi menggunakan protokol yang disyorkan didokumentasikan pada tahap awal kajian. Ini

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dihapuskan dengan menurunkan jumlah *CM* berdasarkan berat badan dan secara beransur-ansur meningkatkan kadar dan tekanan semasa infus. Seluruh badan dianalisis berdasarkan sistem anatomi dan penemuan PMCT / PMCTA berbanding dengan autopsi. Nilai koefisien persamaan @ similarity coefficient (SC) 0.876 untuk semua 3660 pemboleh ubah yang dianalisis dan signifikan secara statistik menunjukkan korelasi yang kuat. Sistem vaskular mempunyai korelasi terkuat. COD yang paling banyak adalah kematian kardiovaskular. 78.3% sepadan, 15.0% kecil dan 6.67% perbezaan COD utama antara ahli radiologi dan ahli patologi. Hubungan yang kuat bagi kedua ahli radiologi (SC: 0,867 hingga 0,883) tetapi lebih rendah sedikit jika dibandingkan dengan ahli patologi (nilai SC: 0,767). Ujian hipotesis menunjukkan hasil yang signifikan dan menyimpulkan bahawa terdapat kesimpulan hubungan atau kesamaan pada COD antara ahli radiologi dan ahli patologi. CL untuk ahli radiologi pada umumnya lebih rendah berbanding dengan ahli patologi. CL tertinggi adalah dalam mendiagnosis patologi vaskular. PMCTA meningkatkan CL mereka dan membantu dalam COD mereka berbanding dengan PMCT sahaja. Majoriti masih memerlukan autopsi penuh atau terhad.

Kesimpulannya Protokol PMCTA yang baru diubah suai untuk penduduk Asia yang menggunakan pendekatan leher telah terbukti secara saintifik dan statistik dengan nilai diagnostik yang tinggi dan hasil yang menjanjikan. COD ahli radiologi berdasarkan PMCT / PMCTA adalah setanding dengan autopsi terutamanya dalam patologi berkaitan vaskular. Peranan pengimejan forensik di Malaysia, kekal sebagai tambahan untuk autopsi dan tidak menggantinya sepenuhnya dengan potensi tinggi untuk autopsi terhad pada masa akan datang.

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A/P Dr Haji Saiful Nizam bin Haji Abdul Rashid

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LIST OF ABBREVIATIONS

A&E	Accident & Emergency
AL	Autopsy body length
AP	Arterial phase
AVM	Arteriovenous malformation
AW	Autopsy body weight
BID	Brought in dead
C&S	Culture and sensitivity
CAD	Coronary artery disease
CCA	Common Carotid Artery
CL	Confident level
CM	Contrast media
CNS	Central nervous system
COD	Cause of death
COW	Circle of Willis
CPR	Cardiopulmonary resuscitation
CS	Chi-Squared Value
CU	Genitourinary system
CVD	Cardiovascular disease
CVL	Central line insertion
DCS	Data Collection Sheet
Df	Degree of Freedom
DHF/DSS	Dengue Hemorrhagic fever/ Dengue shock syndrome
DHS	Dynamic hip screw

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DNA	Deoxyribonucleic acid
DP	Dynamic phase
DVDs	Digital versatile disc
DVT	Deep venous thrombosis
FN	False negative
FP	False positive
GIT	Gastrointestinal system
HKL	Hospital Kuala Lumpur
HPE	Histopathological examination
HU	Hounsfield Unit
ICB	Intracranial bleed
ICD-10-CM	International Classification of Diseases, Tenth Revision, Clinical Modification
ICU	Intensive Care Unit
IHD	Ischemic heart disease
IJV	Internal Jugular Vein
IT	Information technology
JAKIM	Jabatan Kemajuan Islam Malaysia
KKM/MOH	Kementerian Kesihatan Malaysia/ Ministry of Health
KVP	Kilovoltage peak
LAD	Left ascending artery
LCX	Left circumplex artery
LPO	Left anterior oblique
mAs	Milliampere-seconds
MIP	Maximum intensity projection

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MOSTI	Ministry of Science, Technology and Innovation
MPR	Multiplanar reconstructions
MREC	Medical Research Ethics Committee
MRI	Magnetic resonance imaging
MSCT	Multislice computed tomography
MVA	Motor vehicle accidents
NCD	Non-communicable Diseases
NIFM/IPFN	National Institute of Forensic Medicine/ Institut Perubatan Forensik Malaysia,
NMRR	National Medical Research Register
PACS	Picture archiving and communications system
Path	Pathologist
PE	Pulmonary embolism
PEG	Polyethylene Glycol
PMCT	Postmortem Computed Tomography
PMCTA	Postmortem Computed Tomography Angiography
PMI	Post-mortem interval
PMMR	Postmortem magnetic resonance
Rad 1	Radiologist 1
Rad 2	Radiologist 2
RCA	Right coronary artery
RCT	Randomized control trial
RPO	Right posterior oblique
SAH	Subarachnoid bleed
SC	Similarity Coefficients

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SD	Sudden death
SDH	Subdural hemorrhage
SDR	Sudden death related
SND	Sudden Natural Death
SOB	Shortness of breath
SOP	Standard operating procedure
SPSS	Statistical Package for the Social Sciences
SVC	Superior vena cava
TN	True negative
TOD	Time of death
TP	True positive
UPM	Universiti of Putra Malaysia
VIFM	Victoria Institute of Forensic Medicine
VP	Venous phase
VRT	Volume-rendering technique
WHO	World Health Organization

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CHAPTER 1

INTRODUCTION

1.1 Background of the Research

Postmortem computed tomography (PMCT) was introduced in our mortuary in 2009 as an adjunct to autopsy but with limitation in vascular and organs opacification. Therefore, postmortem computed tomography angiography (PMCTA) was introduced to overcome these limitations. However, the reliability and effectiveness of PMCTA has never been tested in our center especially on Asian population as previous PMCTA protocol was designed for larger and heavier Western population.

Whole body PMCTA commonly used groin or femoral approach and neck approach was only used for selective PMCTA. However, it is more feasible to use neck approach in our center as the cut down was conducted by forensic pathologists with no additional incision on the body. Whole body PMCTA using neck approached on large scale study has never been done or proven scientifically. Sudden natural death (SND) was chosen as it is the commonest cause of death (COD) in our mortuary and research in this area is limited.

The purpose of this study was to design a new PMCTA protocol dedicated for Asian population based on body weight and test its reliability in terms of diagnostic value for organ and vascular pathology in comparison to autopsy, assess its potential in diagnosing the possible COD in comparison to pathologist's COD and documented complications and pitfalls. The radiologists and pathologists' confident level (CL) in formulating their COD, decision on whether autopsy is needed or not, PMCTA helps in their COD and if PMCTA increased their confident level compared to PMCT alone were assessed.

1.1.1 Sudden natural death

A death by natural causes, as recorded by authorities and on death certificates and associated documents, is one that is primarily attributed to an illness or an internal malfunction of the body not directly influenced by external forces. Sudden death (SD) or sudden unexpected death is defined as sudden death of an individual who appears healthy and dies suddenly within a few minutes or several hours due to pre-existing disease or functional disorder. The official definition of SD as described by World Health Organization (WHO) is that an individual die of natural diseases within 24 hours since symptoms appear (ICD-10; code No. 96).

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Diseases of any physical systems may lead to sudden unexpected death. In Malaysia, SD with medico-legal implications subjected to a postmortem request by the Police Department can be categorized into three major categories such as accidental, homicide /suicide and natural death. Sudden Natural Death (SND) is defined as non-trauma associated deaths where there is evidence or not of previous illnesses.

Cardiovascular disease (CVD) is the most frequent culprit behind the occurrence of SND cases worldwide and in Malaysia which include coronary artery disease, hypertensive heart disease and primary myocardial disease (Amplavanar *et al.*, 2010; KKM Health Facts, 2019). The other causes are central nervous system ailments (ruptured berry aneurysm and cerebral hemorrhage) and respiratory system diseases (pulmonary embolism and bleeding from tumour or pulmonary tuberculosis). The least common causes are gastrointestinal system diseases which include bleeding peptic ulcers and Genitourinary/Reproductive system diseases like acute pyelonephritis with sepsis and ruptured ectopic pregnancy (Nagata *et al.*, 2013) (refer Table 1.1).

The principal cause of death in Malaysia released by World Health Organization – Non-communicable Diseases (NCD) Country Profiles, (2016) was cardiovascular diseases (35.8%) for both gender and population aged from 15 years old and beyond (KKM Health Facts, 2019) The main cause of SND in Ministry of Health (MoH) hospitals (2019) was ischemic heart disease with 15.6 % (KKM Health Facts, 2019). In Hospital Kuala Lumpur (HKL), 744 autopsies were done in 2017 from a total of deaths 3470 (21.44%) with 480 cases (64.52 %) were SND cases.

Table 1.1 : 5 principle cause of sudden natural death in Malaysian Hospital (2019) based on KKM Health Facts, 2019

No.	Type of Disease	Percentage (%)
1	Ischemic heart diseases	15.9
2	Pneumonia	11.5
3	Cerebrovascular diseases	7.3
4	Transport accidents	3.5
5	Malignant neoplasm of trachea, bronchus and lung	2.6

1.1.2 Postmortem Computed Tomography in Malaysia

Public objection to autopsy due to cultural and mainly religious beliefs especially among the Muslim community is well known not just in Malaysia but also worldwide (Nadesan, 1997). There is an increasing awareness and demand by the Malaysian public for a minimally invasive alternative to autopsy.

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Forensic radiology is a fusion of radiological imaging utilizing radiographic, computed tomography, angiography and magnetic resonance imaging (MRI) techniques with post-mortem pathology (O'Donnell & Woodford, 2008). Forensic radiology is relatively new in Malaysia with only three (3) radiologists have proper forensic radiology training but fortunately they are supported by a strong team of radiographers and with a dedicated 64-slice, multislice computed tomography (MSCT) within the mortuary complex at the National Institute of Forensic Medicine (NIFM) or *Institut Perubatan Forensik Malaysia (IPFN)*, Hospital Kuala Lumpur (HKL). This center was established in 2009 as a research center with Universiti Putra Malaysia (UPM) and Universiti Institut Teknologi Malaysia (UITM) collaboration to study the implication and prospect of Forensic Radiology in our mortuary system. In 2017, 744 cadavers were scanned prior to autopsy and 576 cadavers in 2018. Majority of these cases are SD cases including natural, trauma, motor vehicle accidents (MVA), gunshot wound, stab wound, suicide, asphyxia, drowning, burn and poisoning. There are also cases related to drug mules and intoxication (Rashid *et al.*, 2013) .

Currently in NIFM (HKL), PMCT has been used as an adjunct to autopsy since 2009. Each corpse which requires autopsy will be admitted to the mortuary and scanned. The PMCT will be reviewed by the forensic radiologist and findings will be discussed with the forensic pathologist prior to autopsy. Although PMCT role as an adjunct to conventional autopsy is well established and accepted especially in traumatic death (Hoey *et al.*, 2007), yet the extent of the role as potential replacement to the invasive autopsy remains unclear due to its limitation in the diagnosis of natural death, especially in SND (Roberts *et al.*, 2012; Le Blanc-Louvry *et al.*, 2013; Chevallier C *et al.*, 2013)

The scanning protocols were adapted from Victoria Institute of Forensic Medicine (VIFM) Australia and *Virtopsy*® Team, Institute of Forensic Medicine, University of Zurich, Zurich, Switzerland. These scanning protocols have never been tested or validated in Malaysia. In VIFM, the bodies are scanned in two blocks, head and neck, and upper thorax until the toe with the upper limbs by the side (Amplavanar *et al.*, 2010 ;Grabherr *et al.*, 2008) while the *Virtopsy*® Team scanned the bodies in a single block (head to toe) with the upper limbs elevated (Flach *et al.*, 2014). No large-scale study has been done in Malaysia to validate the effectiveness and reliability of these PMCT scanning protocols in the cause of death particularly in sudden natural death.

Furthermore, despite the advantages of PMCT in terms of its performance simplicity, data acquisition and cost effectiveness, this technique has the disadvantage of limited organ parenchyma and vascular system visualization (Le Blanc-Louvry *et al.*, 2013; Roberts *et al.*, 2012; Chevallier C *et al.*, 2013).

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1.1.3 Postmortem Computed Tomography Angiography in Malaysia

PMCTA techniques have been developed to overcome the limitations and increase the diagnostic value of PMCT (Grabherr *et al.*, 2008; Ross *et al.*, 2008; Grabherr *et al.*, 2010). There are numerous publications on comparison between PMCT and PMCTA findings with conventional autopsy. However, majority of these publications were on based on single case study (Abdul Rashid, Bouwer & O'Donnell, 2012; Bott, O'Donnell & Burke, 2013; Rashid *et al.*, 2013) or small sample population(Levy *et al.*, 2007; Rutty & Swift, 2004; Thali *et al.*, 2003; Grabherr *et al*., 2018). There are many different PMCTA techniques described in literature but there is no single technique appears to be the gold standard. They vary from selective single organ system to whole body angiography (Robinson *et al.*, 2013). Femoral artery and vein approach is an established and well accepted approach for PMCTA cannulation. Some centers prefer oil-based contrast solution over water-based contrast solution but each with its own advantages and disadvantages (Grabherr *et al.*, 2008; Ross *et al*., 2008; Ampanozi G *et al*., 2020).

Furthermore, majority of PMCT and PMCTA researches and publications were based on western population. Currently, there are limited numbers of research and publications focusing on Asian population (Kasahara *et al.*, 2012) and most publications were based on single case study or reviews (Abdul Rashid *et al.*, 2012; Hoey *et al.*, 2007; Le Blanc-Louvry *et al*., 2013; Rashid *et al*., 2013; Roberts *et al*., 2012). The current scanning protocol for both PMCTA was adapted from *Virtopsy*® Team, Institute of Forensic Medicine, University of Zurich, Zurich, Switzerland and VIFM, Australia. Therefore, researches and publications using Asian population particularly Malaysian samples need to be done in order to assess the feasibility of both PMCT and PMCTA as either an adjunct, limited and even if possible, to replace autopsy.

Although the 'groin approach' using femoral artery and vein is the established and well accepted approach for PMCTA cannulation in whole body postmortem angiogram, there could be cultural or religious issues related to the additional incision made on to the groin region of the deceased in our country. Therefore, an alternative approach was considered. 'Neck approach' using Carotid Artery (CA) and Internal Jugular Vein (IJV) was used by Prof Guy Rutty and his team (Robinson *et al.*, 2013) but this was for selective cardiac angiogram. The effectiveness of this method in whole body postmortem angiogram has never been tested scientifically in a large-scale study. Therefore, this approach is preferable over the groin approach as the catheters can be inserted via the 'Y' incision of the neck with no additional incision needed. Some forensic radiology centers prefer oil-based contrast solution over water-based contrast solution but each with its own advantages and disadvantages (Grabherr *et al*., 2008; Ross *et al*., 2008; Grabherr *et al.* 2010). Water based contrast solution is used in both *Virtopsy* ® and VIFM. For the purpose of this research, their scanning and PMCTA protocol will be adapted. Furthermore, water-based contrast solution is cheaper, and widely available in Malaysia compared to oil-based contrast solution. There is an established and well accepted PMCTA protocol available based on previous studies (Grabherr *et al.*, 2008; Ross *et al*., 2008; Grabherr *et al.* 2010). However, the ratio and amount of solution used, the rate and pressure of the infusion was based on western population and using groin approach. The feasibility of this PMCTA protocol for neck approach and on Asian

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population was studied. The pitfalls and complications related to this approach were observed and evaluated.

Further research needs to be done in order to prove the reliability and validity of PMCT and PMCTA in the diagnosis of cause of SD, particularly SND in Malaysia. Based on these facts, the diagnosis of the cause of SND based on PMCT and PMCTA and its correlation to autopsy were assessed and validated.

1.2 Statement of the problem

In NIFM (HKL), PMCT currently acts as an adjunct to autopsy since 2009. PMCTA is relatively new technique in the field of forensic radiology and has never been practiced in Malaysia. The diagnostic value of the PMCT and PMCTA in terms of scanning protocol, angiographic procedure, images and findings in the diagnosis of SND has never been tested and proven scientifically in Malaysia. The validity of PMCT alone or together with PMCTA in identifying the pathologies and organs involved and the correlation with autopsy in the diagnosis of SND in a predominantly Asian population has never been done previously. Furthermore, the effectiveness of current PMCTA protocol and neck approach in whole body post mortem angiogram and the used of water based contrast solution in Asian population have never been tested scientifically. The assessment of confident level and problems encountered with PMCT alone or together with PMCTA among the forensic radiologists and forensic pathologists in the diagnosis of cause of death (COD) for SND need to be assessed scientifically.

1.3 Research Questions

Could the modified PMCTA protocol dedicated for Asian population based on body weight and using neck approach helps radiologists in formulating their COD in SND which are comparable to autopsy?

1.4 General objective

The goal of this study was to determine the reliability and effectiveness of PMCT/PMCTA in the COD of SND in comparison to autopsy.

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1.5 Specific objectives

1. To test and validate the current scanning protocol of PMCT and PMCTA. A new scanning protocol will be derived at the end of the study.
2. To assess the effectiveness and reliability of the 'neck approach' in whole body postmortem angiogram using recommended 'groin approach' PMCTA protocol as well as documenting possible pitfalls and complications related to neck approach. A new PMCTA cut down and infusion protocol will be derived at the end of the study.
3. To identify the possible pathologies and organs involved and contributed to the COD of SND based on PMCT/PMCTA and their correlation to autopsy.
4. To determine the concordance/discordant of COD of SND diagnosed on PMCT/ PMCTA and autopsy.
5. To determine the interobserver agreement between radiologists and to assess their confident level in the diagnosis of COD of SND based on PMCT/PMCTA findings.
6. To assess the forensic pathologist's confident level in the diagnosis of COD of SND based on autopsy and to document any problem related to the utilization of PMCTA contrast media encountered during autopsy.

1.6 Research hypothesis

The null hypothesis is: There is no relationship between the radiologist's COD of SND based on PMCT/PMCTA and forensic pathologist's COD of SND based on autopsy.

The alternative hypothesis is: There is relationship between the radiologist's COD of SND based on PMCT/PMCTA and forensic pathologist's COD of SND based on autopsy.

1.7 Significance of the study

Results from this study would be important to the cultural, religious and legal system as it will determine whether PMCT alone or PMCT together with PMCTA will increase the diagnostic value in the diagnosis of the COD of SND and could completely replace autopsy or at least complement a limited autopsy. It will possibly determine its capacity as evidence in the court of law in Malaysia. If the outcomes of the study if fruitful and excepted by the forensic pathologists and our legal system, this will definitely lead to change in the conduct of death investigation and improve the quality of mortuary services in not only in NIFM, HKL but in the whole nation. I would like to prove scientifically that PMCT together with PMCTA using 'neck approach' and a modified PMCTA infusion protocol as well as scanning protocol based on body weight could be introduced and practiced in Malaysia's mortuaries or even introduced to other countries. The outcomes of this research will enhance further research in the field of forensic radiology in Malaysia and across its borders.

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1.8 Limitation of research

Some of the limitations of our study included pediatric population is excluded, only fresh sample of less than 24 hours and cases with suspected contagious disease, example; Pulmonary Tuberculosis, HIV and Hep B are excluded.

1.9 Thesis outline

In this research, the chapter arrangement will be as follows:

Chapter 1: The first chapter introduces the subject matter, the background to of the research, problem statement, the research objectives, scope of the research and the significance of the research.

Chapter 2: The second chapter will discuss the previous studies done on the research. There will be a summarized tabular presentation of previous research on this subject.

Chapter 3: This chapter will explain and describe the procedure and methods used in this study.

Chapter 4 & 5: This chapter will display and discuss the results of the analysis obtained in chapter 3. The results obtained here will be compared the results of some of the previous studies and inferences will be drawn.

Chapter 6: This last chapter will end the study with a brief discussion of the conclusion, contributions of the study and some recommendations for further research on the topic.

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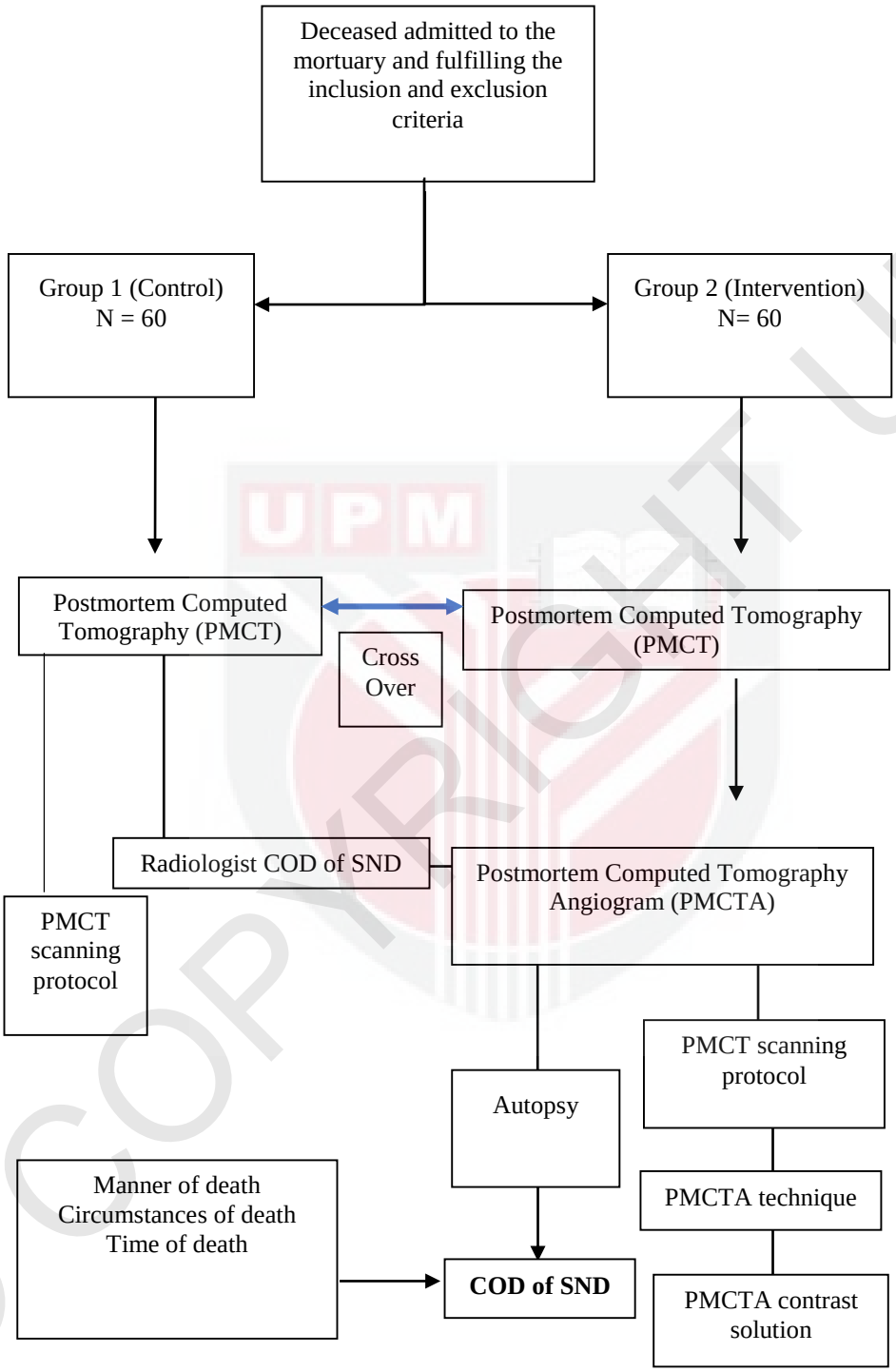

Figure 1.1 : Conceptual Framework of RCT

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REFERENCES

[1.] International Statistical Classification of Diseases and Related Health Problems 10th Revision. ICD-10 Version (2016).

[2.] N T Amplavanar et al (2010). Prevalence of Cardiovascular Disease Risk Factors Among Attendees of the Batu 9, Cheras Health Centre, Selangor, Malaysia. *Med J Malaysia*, 65: 166-172.

[3.] Health Facts (2017). www.moh.gov.my.

[4.] Hisayama, Nagata M, Ninomiya T, Doi Y, Hata J, Ikeda F, Mukai N, Tsuruya K, Oda Y, Kitazono T, Kiyohara. (2013) Temporal trends in sudden unexpected death in a general population. *Am Heart J*, Jun;165(6):932-938.e1. doi: 10.1016/j.ahj.2013.02.028.

[5.] Chris O'Donnell and N. Woodford. (2008). Post-mortem Radiology – A new sub-specialty?. *Clinical Radiology*, Vol 63: 1189 – 1194.

[6.] Hoey BA, Cipolla J, Grossman MD, McQuay N, Shukla PR, Stawicki SP, Stehly C,Hoff WS. (2007). Postmortem computed tomography, "CATopsy", predicts cause of death in trauma patients. *J Trauma*, Nov; 63(5):979-85; discussion 985-6.

[7.] Le Blanc-Louvry I, Thureau S, Duval C, Papin-Lefebvre F, Thiebot J, Dacher JN, Gricourt C, Touré E, Proust B. (2013). Post-mortem computed tomography compared to forensic autopsy findings: a French experience. *Eur Radiol*, Mar 12.

[8.] Roberts IS, Benamore RE, Benbow EW, Lee SH, Harris JN, Jackson A, Mallett S, Patankar T, Peebles C, Roobottom C, Traill ZC. (2012). Post-mortem imaging as an alternative to autopsy in the diagnosis of adult deaths: a validation study. *Lancet*, Jan 14;379(9811):136-42. doi: 10.1016/S0140-6736(11)61483-9.

[9.] Grabherr S, Gygax E, Sollberger B, Ross S, Oesterhelweg L, Bolliger S, Christe A, Djonov V, Thali MJ, Dirnhofer R. (2008). Two-step postmortem angiography with a modified heart-lung machine: preliminary results. *AJR Am J Roentgenol*, Feb;190(2):345-51. doi: 10.2214/AJR.07.2261.

[10.] Ross S, Spendlove D, Bolliger S, Christe A, Oesterhelweg L, Grabherr S, Thali MJ, Gygax E. (2008). Postmortem whole-body CT angiography: evaluation of two contrast media solutions. *AJR Am J Roentgenol*. May;190(5):1380-9. doi: 10.2214/AJR.07.3082.

[11.] Abdul Rashid SN, Krauskopf A, Vonlanthen B, Thali MJ, Ruder TD Sudden death in a case of sickle cell anemia: Post-mortem computed tomography and autopsy correlation from a radiologist's perspective. (2013). *Leg Med (Tokyo)*, Feb 26. pii: S1344-6223(13)00006-0. doi: 10.1016/j.legalmed.2013.01.003.

© COPYRIGHT UPM

[12.] Rashid SN, Bouwer H, O'Donnell C. (2012). Lethal hemorrhage from a ureteric-arterial-enteric fistula diagnosed by postmortem CT angiography. *Forensic Sci Med Pathol*, Dec;8(4):430-5. doi: 10.1007/s12024-012-9332-3. Epub 2012 Apr 4.

[13.] Bott E, O'Donnell C, Burke M. Post mortem CT demonstration of hemoperitoneum caused by rupture of a paraumbilical vein into a paraumbilical hernia in a man with liver cirrhosis and portal hypertension. (2013). *Forensic Sci Med Pathol*, Mar;9(1):77-81. doi: 10.1007/s12024-012-9384-4.

[14.] Rutty GN, Swift B. (2004). Accuracy of magnetic resonance imaging in determining cause of sudden death in adults:comparison with conventional autopsy. *Histopathology*, Feb;44(2):187-9.

[15.] Michael J Thali, K Yen, W Schweitzer, et al. (2003). Virtopsy, a new imaging horizon in Forensic Pathology : Virtual autopsy by post-mortem multislice computed tomography (MSCT) and magnetic resonance imaging (MRI) – a feasibility study. *Journal of Forensic Science*, Vol 48 : 386 – 403.

[16.] Levy G, Goldstein L, Blachar A, Apter S, Barenboim E, Bar-Dayan Y, Shamis A, Atar E. (2007). Postmortem computed tomography in victims of military air mishaps: radiological-pathological correlation of CT findings. *Isr Med Assoc J*, Oct; 9(10):699-702.

[17.] Bin Abdul Rashid SN, Rahim AS, Thali MJ, Flach PM. Death by 'ice': fatal methamphetamine intoxication of a body packer case detected by postmortem computed tomography (PMCT) and validated by autopsy. (2013). *Forensic Sci Med Pathol*, Mar;9(1):82-7. doi: 10.1007/s12024-012-9395-1.

[18.] Poulsen K, Simonsen J. (2007). Computed tomography as routine in connection with medico-legal autopsies. *Forensic Sci Int*, Sep 13;171(2-3):190-7.

[19.] Chris O'Donnell, A. Rotman and S. Collett. (2007). Current Status of Routine Post-mortem CT in Melbourne. *Forensic Science Medicine Pathology*, Vol 3: 226 -232.

[20.] Thali MJ, Jackowski C, Oesterhelweg L, Ross SG, Dirnhofer R. (2007). VIRTOPSY - the Swiss virtual autopsy approach. *Leg Med (Tokyo)*, Mar;9(2):100-4.

[21.] Nadesan K. (1997). The importance of the medico-legal autopsy. *Malays J Pathol*, Dec;19(2):105-9.

[22.] J Roulson, E W Benbow & P S Hasleton. (2005). Discrepancies between clinical and autopsy diagnosis and the value of post mortem histology; a meta-analysis and review. *Histopathology*, 47, 551–559. DOI: 10.1111/j.1365-2559.2005.02243.x

© COPYRIGHT UPM

[23.] Geller SA. (1984). Religious attitudes and the autopsy. *Arch Pathol Lab Med*. Jun;108(6):494-6.

[24.] Gatrad AR. (1994). Muslim customs surrounding death, bereavement, postmortem examinations, and organ transplants. *BMJ*. Aug 20-27;309(6953):521-3.

[25.] Fatwa-kebangsaan/hukum-menggunakan-kaedah-autopsi-maya-sebagai-alternatif-kepada-bedah-siasat-mayat.(2016). http://www.islam.gov.my/images/ePenerbitan/KOMPILASI_MUZAKARAH_MKI.

[26.] Benjamin Swift and Guy N. Rutty. (2008). Recent Advances in Postmortem Forensic Radiology: Computed Tomography and Magnetic Resonance Imaging Applications. *Forensic Pathology Reviews*, Vol 4: 355 – 404.

[27.] Tzipi Kahana and Jehuda Hiss. (2007). Forensic Radiology. *Forensic Pathology Reviews*, Vol 3: 443 – 460. .

[28.] Thali MJ, Brogdon BG, Viner MD, eds. (2010). Forensic Radiology. 2nd ed. Boca Raton, Fla: CRC Press.

[29.] Thali MJ, Jackowski C, Oesterhelweg L, Ross SG, Dirnhofer R. (2007). VIRTOPSY - the Swiss virtual autopsy approach. *Leg Med (Tokyo)*, Mar;9(2):100-4.

[30.] Shiotani S, Shiigai M, Ueno Y, Sakamoto N, Atake S, Kohno M, Suzuki M, Kimura H, Kikuchi K, Hayakawa H. (2008). Postmortem computed tomography findings as evidence of traffic accident-related fatal injury. *Radiat Med*,Jun;26(5):253-60. doi: 10.1007/s11604-007-0223-6.

[31.] Kasahara S, Makino Y, Hayakawa M, Yajima D, Ito H, Iwase H. (2012). Diagnosable and non-diagnosable causes of death by postmortem computed tomography: a review of 339 forensic cases. *Leg Med (Tokyo)*, Sep;14(5):239-45. doi: 10.1016/j.legalmed.2012.03.007.

[32.] Katarzyna Michaud, Silke Grabherr, Francesco Doenz, Patrice Mangin. (2012). Evaluation of postmortem MDCT and MDCT-angiography for the investigation of sudden cardiac death related to atherosclerotic coronary artery disease. *Int J Cardiovasc Imaging*, DOI 10.1007/s10554-012-0012-x

[33.] Aghayev E, Sonnenschein M, Jackowski C, Thali M, Buck U, Yen K, Bolliger S, Dirnhofer R, Vock P. (2006). Postmortem radiology of fatal hemorrhage: measurements of cross-sectional areas of major blood vessels and volumes of aorta and spleen on MDCT and volumes of heart chambers on MRI. *AJR Am J Roentgenol*, Jul;187(1):209-15.

© COPYRIGHT UPM

[34.] Kennedy D, Laing C, Tseng L et al. (2010). Detection of active gastrointestinal hemorrhage with CT angiography: a 4(1/2)-year retrospective review. *J Vasc Interv Radiol*, 21(6):848–855.

[35.] Karhunen PJ, Servo A. (1993). Sudden fatal or non-operable bleeding from ruptured intracranial aneurysm: evaluation by post-mortem angiography with vulcanising contrast medium. *Int J Legal Med*, 106(2):55–59.

[36.] Roberts I, Benamore R, Peebles C et al. (2011). Diagnosis of coronary artery disease using minimally invasive autopsy: evaluation of a novel method of post-mortem coronary CT angiography. *Clin Radiol*, 66(7):645–650, *Technical report Int J Legal Med*.

[37.] Saunders S, Morgan B, Raj V et al. (2011). Targeted post-mortem computed tomography cardiac angiography: proof of concept. *Int J Legal Med*, 125(4):609–616.

[38.] Jackowski C, Thali M, Sonnenschein M et al. (2005). Virtopsy: postmortem minimally invasive angiography using cross section techniques—implementation and preliminary results. *J Forensic Sci*, 50(5):1175–1186.

[39.] Grabherr S, Djonov V, Friess A et al. (2006). Postmortem angiography after vascular perfusion with diesel oil and a lipophilic contrast agent. *AJR*, 187(5):W515–W523.

[40.] Kominato Y, Fujikura T, Hata Y et al. (2006). A case of postoperative haemorrhage after a hysterectomy in which a bleeding point of the left uterine artery was identified by postmortem angiography. *Legal Med*, 6(3):187–189.

[41.] Ruder T, Ketterer T, Preiss U et al. (2011). Suicidal knife wound to the heart: challenges in reconstructing wound channels with postmortem CT and CT-angiography. *Legal Medicine*, 13(2):91–94.

[42.] Sakamoto N, Senoo S, Uemura Y et al. (2009). Case report: cardiopulmonary arrest on arrival case which underwent contrast-enhanced post-mortem CT. *KANTO. J Japanese Association Acute Med*, 30:114–115.

[43.] Lizuka K, Sakamoto N, Kawasaki H, Miyoshi T, Komatuzaki A, Kikuchi S. (2009), Usefulness of contrast-enhanced post-mortem CT. *Innervision*, 24:89–92.

[44.] Grabherr S, Djonov V, Yen K, Thali MJ, Dirnhofer R. (2007). Postmortem angiography: review of former and current methods. *Am J Roentgenol*, 188:832–838.

[45.] Jackowski C, Persson A, Thali MJ. (2008). Whole body post-mortem angiography with a high viscosity contrast agent solution using poly ethylene glycol as contrast agent dissolver. *J Forensic Sci*,53:465–468.

© COPYRIGHT UPM

[46.] Grabherr S, Doenz F, Steger B, Dirnhofer R, Dominguez A,Sollberger B et al. (2010). Multi-phase post-mortem CT angiography:development of a standardized protocol. *Int J Legal Med*, 125:791–802.

[47.] Rutty GN, Saunders S, Morgan B, Raj V. (2012). Targeted cardiac post-mortem computed tomography angiography: a pictorial review. *Forensic Sci Med Pathol*, 8:40–47.

[48.] Roberts ISD, Benamore RE, Peebles C, Roobottom C, Traill ZC. (2011). Diagnosis of coronary artery disease using a minimally invasive autopsy: evaluation of a novel method of post-mortem coronary CT angiography. *Clin Radiol*, 66:645–650.

[49.] Chevallier Christine & Doenz Francesco & Vaucher Paul & Palmiere Cristian & Dominguez Alejandro & Binaghi Stefano & Mangin Patrice & Grabherr Silke. (2013). Postmortem computed tomography angiography vs. conventional autopsy: advantages and inconveniences of each method. *Int J Legal Med*, 127:981–9892013.

[50.] Claire Robinson & Jade Barber & Jasmin Amoroso & Bruno Morgan & Guy Rutty. (2013) .Pump injector system applied to targeted post-mortem coronary artery angiography. *Int J Legal Med*, 127:661–666.

[51.] Silke Grabherr, Christèle Widmer, Katia Iglesias, Frank Sporkert, Marc Augsburger, Patrice Mangin and Cristian Palmiere. (2012). Postmortem biochemistry performed on vitreous humor after post-mortem CT-angiography. *Legal Medicine*, 14 297–303.

[52.] G.N. Rutty, P. Smith, T. Vissera, J. Barber, J. Amorosa and B. Morgan. (2013). The effect on toxicology, biochemistry and immunology investigations by the use of targeted post-mortem computed tomography angiography. *Forensic Science International*, 225 42–47.

[53.] Flach PM1, Gascho D, Schweitzer W, Ruder TD, Berger N, Ross SG, Thali MJ, Ampanozi G. (2014). Imaging in forensic radiology: an illustrated guide for postmortem computed tomography technique and protocols. *Forensic Sci Med Pathol*, Dec;10(4):583-606. doi: 10.1007/s12024-014-9555-6.

[54.] Suzuki H, Hasegawa I, Hoshino N, Fukunaga T. (2015). Two forensic autopsy cases of death due to upper gastrointestinal hemorrhage: A comparison of postmortem computed tomography and autopsy findings. *Leg Med (Tokyo)*, May;17(3):198-200. doi: 10.1016/j.legalmed.2014.12.010.

[55.] Filograna L, Thali MJ, Marchetti D. (2014). Forensic relevance of post-mortem CT imaging of the haemopericardium in determining the cause of death. *Leg Med (Tokyo)*, Sep;16(5):247-51. doi: 10.1016/j.legalmed.2014.05.005.

© COPYRIGHT UPM

[56.] Silke Grabherr, Axel Heinemann, Hermann Vogel, Guy Rutty, Bruno Morgan, Krzysztof Woźniak, Fabrice Dedouit, Florian Fischer, Stefanie Lochner, Holger Wittig, Giuseppe Guglielmi, Franziska Eplinius, Katarzyna Michaud, Cristian Palmiere, Christine Chevallier, Patrice Mangin, Jochen M. Grimm. (2018). Postmortem CT Angiography Compared with Autopsy: A Forensic Multicenter Study. *Radiology*,Jul;288(1):270-276. doi: 10.1148/radiol.2018170559.

[57.] Garyfalia Ampanozi, Delaja Halbheer, Lars C Ebert, Michael J Thali, Ulrike Held. (2020). Postmortem imaging findings and cause of death determination compared with autopsy: a systematic review of diagnostic test accuracy and meta-analysis. Int J Legal Med. Jan;134(1):321-337. doi: 10.1007/s00414-019-02140-y.

[58.] Peter Markus Spieth, Anne Sophie Kubasch, Ana Isabel Penzlin, Ben Min-Woo Illigens, Kristian Barlinn and Timo Siepmann. (2016). Randomized controlled trials – a matter of design. *Neuropsychiatr Dis Treat,* 12: 1341–1349. Published online Jun 10. doi: 10.2147/NDT.S101938.

[59.] Kabisch M, Ruckes C, Seibert-Grafe M, et al. (2012). On the proper use of the crossover design in clinical trials: part 18 of a series on evaluation of scientific publications. *Dtsch Arztebl Int,*109:276–281.

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