Detecting the cause of death in infants and children: Whole body post-mortem computed tomography compared to autopsy.

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October 2018

Conferences and publication arising from this thesis

Published paper:

Mohamed Ben Taher; Jean Russell; Marta C Cohen; Amaka C. Offiah (Acceptability of post-mortem imaging among Muslim and non-Muslim communities) has been published in the British Journal of Radiology (BJR)

https://doi.org/10.1259/bjr.20180295

https://www.auntminnie.com/index.aspx?sec=ser&sub=def&pag=dis&ItemID=117701

Paper undergoing peer-review:

Mohamed Ben Taher; Timothy M. Skerry; Jean Russell; Marta C Cohen; Amaka C. Offiah. Non-Invasive Estimation of Post-Mortem Interval using Computed Tomography, Submitted to International Journal of Legal Medicine.

Podium (oral) presentation:

Mohamed Ben Taher; Timothy M. Skerry; Jean Russell; Marta C Cohen; Amaka C. Offiah. Non-Invasive Estimation of Post-Mortem Interval using Computed Tomography. 40th Post Graduate Course & 54th Annual Meeting of the European Society of Paediatric Radiology (ESPR 2018). Abstract published in Pediatric Radiology 2018. 421-422. Berlin. Germany.

Posters:

Mohamed Ben Taher; Marta Cohen; Amaka C Offiah. The role of whole-body post-mortem CT scan in the detection of causes of unexpected infant death. 6th Annual Mellanby Centre Research Day, Sheffield, UK

Mohamed Ben Taher; Marta Cohen; Amaka C Offiah. Is Post-mortem Imaging Acceptable to the Libyan Community? 7th Annual Mellanby Centre Research Day, Sheffield, UK

Mohamed Ben Taher; Marta Cohen; Amaka C Offiah. Is post-mortem imaging acceptable to the Libyan community? UKRC Congress 2017, Manchester, UK.

Mohamed Ben Taher; Timothy M. Skerry; Jean Russell; Marta C Cohen; Amaka C. Offiah. Estimating time of death using post-mortem computed tomography. BSPR National Meeting 2017, Manchester, UK

Acknowledgments

In the name of Allah, the most Gracious, the most Merciful. Thanks be to Allah for giving me enough strength and the blessing to complete this thesis.

First, I would like to express my deepest gratitude to my supervisors, Dr. Amaka C Offiah and Dr. Marta Cohen, for their patience, continuous support and unlimited encouragement throughout my period of study. I would also like to thank them for their help and dedicated involvement in every step of the process of preparing this report. Without their support and guidance more than four years of this study. I would also like to give my gratitude to my main tutor, Dr. Peter S Grabowski, for his supervision during this time. I also appreciate the financial support of the Libyan Ministry of Higher Education.

My appreciation and thanks extend to Elzene Kruger, Jennifer Simpson and the staff of the Department of Radiology, Sheffield Children's Hospital who supported me to finish this study.

My thanks are extended to Dr. Darren Robinson, Light Microscopy Facility Manager, Department of Biomedical Science, who provided me with training in using the ImageJ software to measure air volume.

I would also like to thank my friend Dr. Gnadi Zwawe for helping transport the dead lambs to scan and also for his support during many difficult periods during my study and thesis preparation.

Abstract

Post-mortem investigation is a sensitive issue that needs to be studied in order to address the many issues that surround this topic. This thesis is divided into 7 chapters. Chapter One is a review of the literature, providing information about identifying the causes of death in children, autopsy protocols and the acceptability of post-mortem investigations among the public. Chapter Two determined the reaction towards post-mortem procedures among Muslims and non-Muslims in Libya and in the UK. Muslims were found to have a significant preference for post-mortem imaging compared to autopsy except in homicidal cases. Chapter Three is a systematic review of the literature which identified 3 papers totalling 262 patients and showed overall agreement between post-mortem CT and conventional autopsy of 51%. Chapter Four is an evaluation of the performance of PMCT compared to conventional autopsy in identifying the cause of death in 54 infants and children. Conventional autopsy detected significantly more abnormalities than PMCT and proved to be superior to PMCT for identifying organ' soft tissue abnormalities. PMCT however was superior at identifying skeletal pathology. Chapter Five investigated whether longitudinal changes in organ Hounsfield units (HU) and total body air volume (TBAV) can provide an estimate of post-mortem interval (PMI) in eight euthanised lambs. TBAV increased by 14 cm^3 ($p < 0.001$) for each additional post-mortem day with an intercept of 116 cm^3 ($p < 0.001$). There was clear and progressive decrease in tissue densities and increase in TBAV in individual cases over time. Chapter Six is a pilot study to determine whether PMCT can be used to estimate PMI in 51 infants and children by measuring HU of selected organs. Results suggest that further investigation of the reliability of using HU of the kidney and spleen to estimate PMI is warranted. Chapter Seven provides an overview, discussion and concludes this thesis.

Table of contents

List of Figures

List of Tables

Abbreviations

CT	Computer tomography
CDH	Cumulative degree hours
EV**:	external validity
HU	Hounsfield units
IV*:	internal validity
PM	Post-mortem
PMMRI	Magnetic resonance imaging
NICE	National Institute for Health and Clinical Excellence
PACS	Picture archiving and communication system
PMCT	Post-mortem computed tomography
PMI	Post-mortem interval
SIDS	Sudden infant death syndrome
SUDI	Sudden unexpected death in infancy
3D	Three dimensional
TBAV	Total body air volume

1. Chapter One

1.1 Introduction

The loss of an infant or child is devastating to parents. There were over 5000 children under 19 years of age who died in the UK and Wales in 2017, a 1.6% increase from 2016 (Office for National Statistics, 2017).

. There are multiple causes of death in childhood including injuries, sudden death, endocrine, nutritional and metabolic, cancer, neurological, respiratory, infection, digestive and blood and immune disorders. The most common causes of death in childhood in the UK are injuries, cancer, poisoning, and congenital causes (Wolfe et al., 2014) .

In developing countries, about 12 million infants and children younger than five years old die annually. More than 50% of these deaths are related to diarrhoea, acute respiratory disease, measles or malaria and are conditions that are either treatable or preventable with low-cost interventions. In some developing countries, not all deaths have a clear report about the cause; rather, the number of deaths is compiled from records in which a single direct cause of death is reported (Rice et al., 2000). Trauma causes more than 20,000 childhood deaths annually and about 90% of blunt injuries in childhood are caused by car accidents or falls (Gaines and Ford, 2002). Libya, the home country of this PhD student, is one of these developing countries and in which post-mortem imaging is not currently performed.

Attitudes of the Libyan community to post-mortem in general and post-mortem computed tomography (PMCT) and post-mortem magnetic resonance imaging (PMMRI) in particular have not previously been formally documented. Following the literature review, the first study by this researcher was conducted to ascertain the opinions and preferences of Muslims and non-Muslims regarding PM imaging (PMCT and PMMRI). A qualitative questionnaire-based research study was carried out to measure the attitudes and opinions of Muslims in Libya, Muslims in the UK and non-Muslims in the UK regarding post-mortem (PM) examination. An understanding of this is important as a preliminary step to the long-term goal of introducing PM imaging to Libya and other developing countries.

Post-mortem examination plays an important role in explaining the circumstances of an unexplained death and has been performed for several decades. Autopsy is divided into two parts. The first is the external examination of the body, followed by an internal review, which will open the abdomen, chest cavity and skull (Flach et al., 2014). Leth et al. (2013) highlighted that although the conventional autopsy technique has been improved and developed over the past decades and provide useful information. It is a method that can provide essential information based in many areas of medicine including health care management, medical education and research and quality control and plays an important role in the family's bereavement process (Davies et al., 2004). This information is currently provided by post-mortem examination and is generally considered to be of value when used with chromosomal and genetic studies to counsel parents about risks for future pregnancies (Griffiths et al., 2005). But it has limitations in some body regions such as the spine, neck, face and limbs.

However, autopsy rates across mainland Europe and the UK have been declining for some years (Sieswerda-Hoogendoorn and van Rijn, 2010) (Sieswerda-Hoogendoorn and van Rijn, 2010). UK national data shows that 229,746 deaths were reported to coroners in 2017, the lowest level since 2014. The data also shows a decrease of 5% (11,465) compared to 2016, reflecting the decrease in the number of deaths under

Deprivation of Liberty Safeguards (DoLS) authorisations reported to coroners (National Statistics, 2017).

In most countries, clinical autopsies are performed with permission from the parents of the deceased. Parents should receive suitable, comprehensive and sensitive support in the process of discovering an explanation of the cause of death of their child (Côté, 2010). A forensic investigation may be necessary to identify inflicted causes of death to protect other children and siblings (Côté, 2010). Identifying suspected inflicted injury is a particularly topical and sensitive issue (Kibayashi et al., 2005).

Despite the undisputable utility of autopsy, some families are not willing to give consent for a standard autopsy. Their commonest objection to autopsy is the invasive internal organ examination which they perceive as mutilating the body (Wright and Lee, 2004). Parents also refuse consent for post-mortem examination as they feel that autopsy might not find the cause of death (Rose et al., 2006). Skeletal survey is a fundamentally important process to identify skeletal abnormalities including fractures in post-mortem examination (Olsen et al., 2003). It can be used as evidence of abuse, and may be the only documentation of injury (Offiah and Hall, 2003). Skeletal dysplasias are a large group of genetic conditions which affect bone and cartilage growth and integrity with alterations in shape and size and are also diagnosed from the post-mortem skeletal survey (Victoria et al., 2013). Post-mortem examination and skeletal survey are routinely used at Sheffield Children’s Hospital to detect skeletal abnormalities including skeletal dysplasia.

Alternative or complementary options have been suggested such as post-mortem computed tomography (PMCT), which images the whole body and may be able to diagnose pathology at any anatomical area in the body. Despite the clear benefits of performing autopsies, in the UK more than 50% of parents decline post-mortem (Manktelow et al., 2014). Due to the advances in technology and concerns around declining uptake rates, less invasive methods of autopsy have been developed in recent years such as PMCT and PMMRI (Thayyil et al., 2013).

There are two main methods for cross-sectional post-mortem CT or post-mortem magnetic resonance imaging (PMCT or PMMRI) which are increasingly being used in both the clinical and forensic settings to explain the circumstance and determine the cause of death (Stawicki et al., 2008). Of these, PMCT is less expensive, more widely available and faster to perform, however, it shows poorer soft tissue contrast compared to MRI in fetuses (Arthurs et al., 2016).(Grabherr et al., 2018)

PMCT is mainly used in adults whereas MRI may be more useful in children (Klein et al., 2015). Moreover to being a non-invasive method of investigation, post-mortem imaging has various other advantages that include the opportunity for storing images, the possibility of repetition or reformatting the image, visualisation of non-dissected organs, analysing organs *in situ* and repeating if necessary (Charlier et al., 2012).

The best results in adults have been obtained when combining post-mortem CT angiography with autopsy (Grabherr et al., 2018) and various studies have reported the use of virtual autopsy in adults to explain the circumstances of unexpected death (Thali et al., 2003, Morgan, 2010). However, there have been few studies that focus on post-mortem CT imaging in the paediatric population (Arthurs et al., 2016, Inoue et al., 2014, Proisy et al., 2015, Proisy et al., 2013b) and these have focused on PMCT for identifying causes of sudden death in infants (SIDS) and children. The studies that have been carried out included small numbers of cases and not all cases underwent an autopsy.

Researchers in China have used modern radiological techniques in different fields of forensic science, such as personal identification of bodies, estimation of injury time, determination of the causes of injury, and detection of foreign bodies, but there are only a few studies using medical imaging for estimation of time of death (Wang et al., 2017).

Accurate estimation of the time elapsed since death or the post-mortem interval (PMI) may be a matter of importance in forensic investigations. From the point of view of criminal law, a precise estimation of PMI can help to establish the time of a murder which may then reduce the number of suspects and verify witness statements. PMI is also important in forensic investigations when gathering evidence which may by help to identify the guilty (DiMaio and DiMaio, 2001). Wang et al (2017) used PMCT to evaluate the post-mortem changes in different tissues and organs of rabbits after death and the changing pattern of the average Hounsfield unit (HU) in the organs. Their study analysed the relationship between HU of different organs and PMI. The study showed a negative correlation between the HU of different tissues and organs and the PMI. Their study suggested that increasing the number of organs from which measurements are taken, to evaluate the changes in organs tissue, may improve reliability of PMI estimation.

This researcher carried out two studies related to estimating PMI. The first study observed the dynamic changes of HU of various organs from PM CT images in order to correlate this with PMI in a lamb model. This study also measured total body air volume of each lamb at different times after death.

The second study used post-mortem CT scans of infants and children to estimate PMI by evaluating the changes in HU of different tissues and organs. The scans were reformatted, and the average HU from six sites (brain, heart, lungs, liver, spleen and kidneys) on serial CT images were calculated.

1.1.1 Objectives of the PhD project

1. To determine the opinions towards this procedure among Muslims resident in Libya and Muslims and non-Muslims resident in the UK.
2. Conduct a systematic review to evaluate the extent of agreement between PMCT and conventional autopsy in respect to identifying the causes of death in infants and children.

3. To prospectively compare diagnostic accuracy and evaluate the agreement between PMCT and conventional autopsy for identifying causes of death.

4. To investigate whether longitudinal changes in organ Hounsfield units (HU) and total body air volume (TBAV), as measured from serial PMCT scans, can provide an estimate of PMI.
5. To determine whether organ Hounsfield units (HU) of human tissue can be used to estimate post-mortem interval (PMI).

1.2 Literature review, including methods of diagnosis and autopsy protocols

1.2.1 Diagnosis of causes of death in fetuses, infants and children

1.2.1.1 Fetal deaths

The death of a fetus is an emotionally difficult event for clinicians and the family. Kooper et al. highlighted that fetal death has many different causes, such as fetal-maternal haemorrhage, genetic conditions, placental abnormalities and infections. Different tests to evaluate causes of fetal death, such as perinatal autopsy, cytogenetic analysis, testing for fetal maternal haemorrhage and placental examination can be performed. The first trimester of pregnancy (from fertilisation until the 13th week) has a high rate of spontaneous abortion, with the most common of this being chromosomal abnormality. In second trimester losses, chromosomal anomalies are similar to those found in live births; with trisomy 13, 18, and 21, monosomy X, and sex chromosome polysomies being most common. Second (13–27 weeks) and third trimester (28–42 weeks) fetal deaths may be due to a variety of other single or multiple non-chromosomal causes. Besides fetal abnormalities, placental and cord co-morbidities, or maternal co-morbidities might play a main role, but it can be difficult to find the relationship between cause-and-effect (Kooper et al., 2014).

1.2.1.2 Causes of death in childhood

The death of a child is devastating for the child's parents and family. Almost 3,000 infants died before one year of age in the UK in 2017 and more than 2,000 children died between the ages of 1 and 19 years old (National Statistics, 2017).

The Office for National Statistics states that 61% of deaths occurred before the age of one-year and 18% from 15 to 19 years old. The most common causes of death between the ages of 1 and 4 years old are injuries, cancer, congenital diseases, followed by congenital nervous system and developmental, blood and immune, respiratory, nutritional and metabolic and digestive diseases (Office for National Statistics, 2017).

Another cause of fetal death is skeletal dysplasia. Skeletal dysplasias include osteodystrophies (abnormalities of bone and/or cartilage texture) and dysplasias (abnormalities of bone and/or cartilage growth). Lethal forms may be diagnosed *in utero*, following termination of pregnancy, or perinatally.

Conventional skeletal radiography has been widely used to support paediatric autopsy examination. Skeletal surveys can show bony abnormalities and general bone structure. Skeletal surveys can however be technically difficult to perform due to positional changes with rigor mortis and other artefactual issues, and unlike in live skeletal surveys, there is no standardised protocol or guidance as to when the post-mortem skeletal survey should be used (Office for National Statistics, 2017).

1.2.1.3 Causes of death related to injuries

One of the most common causes of death in childhood after the first year of life is injury. This includes unintentional injury and the failure to decrease unintentional injury deaths during childhood is a pressing concern (Wolfe et al., 2014).

1.2.1.4 Skeletal injury

Fractures are common in inflicted injury and the consequences of misdiagnosing an abusive injury in a child might be grave; incorrectly diagnosing physical abuse in a child whose fractures have another aetiology can have a serious impact on the family (Jenny et al., 1999). Physical abuse may not be included in the physician’s differential diagnosis of childhood injury because the relatives may have intentionally modified the history to conceal the abuse (O'neill et al., 1973). More than 20% of fractures related to child abuse may be missed and are attributed to other causes in children younger than 3 years old (Flaherty et al., 2014). The number of deaths from inflicted injury has been estimated between 2,000 and 5,000 annually (Hilmes et al., 2011). In England and Wales, injury is the second commonest cause of death during childhood (between the ages of 1 and 4 years old) after cancer (Orton et al., 2014). Radiography of the skeleton is always performed in children under two years of age when abuse is suspected or the death was unexpected or accidental (Yildirim et al., 2010). Complete skeletal surveys are used to investigate known and occult fractures particularly in the context of suspected abuse or sudden unexpected death in infancy (SUDI) (Hughes-Roberts et al., 2012). The majority of skeletal trauma in physical abuse involves the skull, limbs and ribs (Ng and Hall, 1998) and fractures are the most common inflicted injury after cutaneous injury and bruising in infants and young children. Recently, autopsy rates have decreased and post-mortem computed tomography (PMCT) has been increasingly used as a supplement to autopsy (Roberts et al., 2012). In the forensic field, PMCT has become a common method for determining the causes of death such as bleeding, fractures or bone abnormalities. PMCT may also help to explain the circumstance of sudden unexpected death and is essential for identifying non-accidental injuries (Proisy et al., 2013a).

The primary method used in the imaging of child abuse remains the skeletal survey as outlined in Royal College of Radiologists and the Society and College of Radiographers guidelines (RCR, 2017). It has been established however that initial skeletal survey might not show acute and nondisplaced fractures, particularly those involving the ribs, and that computed tomography (CT) is more sensitive in identifying rib fractures(Shelmerdine et al., 2018). Several studies suggest that rib fractures may be more common than long bone fractures in children and infants. Studies in recent years have identified rib fractures in infants caused by inflected injury in approximately 80% of cases (Wootton-Gorges et al., 2008). During infancy, rib fractures associated with physical abuse tend to occur in the lateral and posterior arcs of the ribs (Ng and Hall, 1998). A study was carried out by Sanchez et al. in 2015 to identify rib fractures in suspected child abuse. The study retrospectively identified three boys and one girl with suspicion of child abuse from conflicting history from the caregivers and unexplained long bone fractures. The skeletal survey did not show healing rib fractures in any of these cases. The radiologist requested CT scans to exclude occult fractures within 36 hours of the skeletal surveys using their own CT scan protocol with low effective-dose. Their study showed that CT scan showed fractures in the scapula and vertebral body and multiple ribs fracture, which were not identified on the skeletal survey (Sanchez et al., 2015).

Skeletal survey is crucial to consider this possibility when performing a post-mortem examination in sudden unexpected death in infancy and is an important consideration in forensic investigations. It is necessary to take into account possible reasons for such fractures (Schulze et al., 2013). Figure (1.1, Page 24) shows rib fractures on CT with 3D reconstruction.

Fig 1-1. Shows 3D CT Chest: Shows rib fractures

Conversely however, Schulze et al (2013), in their study of 51 forensic cases, identified only 210 rib fractures by PMCT compared to 239 by autopsy. Their study pointed out that CT may not be able to reliably identify rib fractures when there is no displacement (Schulze et al., 2013).

The main weakness with the Schulze et al. (2013) study is that all documentation of autopsy findings and PMCT findings were carried out by the same person. Also, although corpses are handled very carefully when transferred to and from CT, it cannot be excluded that some ribs may have been fractured or existing fractures displaced after the PMCT and were subsequently identified at autopsy – this will be the case for all studies and careful handling will therefore be required during the course of this PhD study.

A chest CT can help to diagnose rib fractures and pneumothoraces (Poulsen and Simonsen, 2007). Poulsen and Simonsen (2007) found that overall, PMCT had a lower sensitivity for rib fracture detection than autopsy, but identified incomplete fractures better than autopsy. They concluded that the detection of rib fractures will increase by using PMCT as a supplement to autopsy.

In the last few years, published PMCT studies have described a specific sort of rib fracture linked with resuscitation attempts called, ‘‘buckle rib fractures’’ (Schulze et al., 2013). Buckle rib fractures are incomplete and exhibit a stable external cortical plate, while the internal cortex often shows changes in alignment.

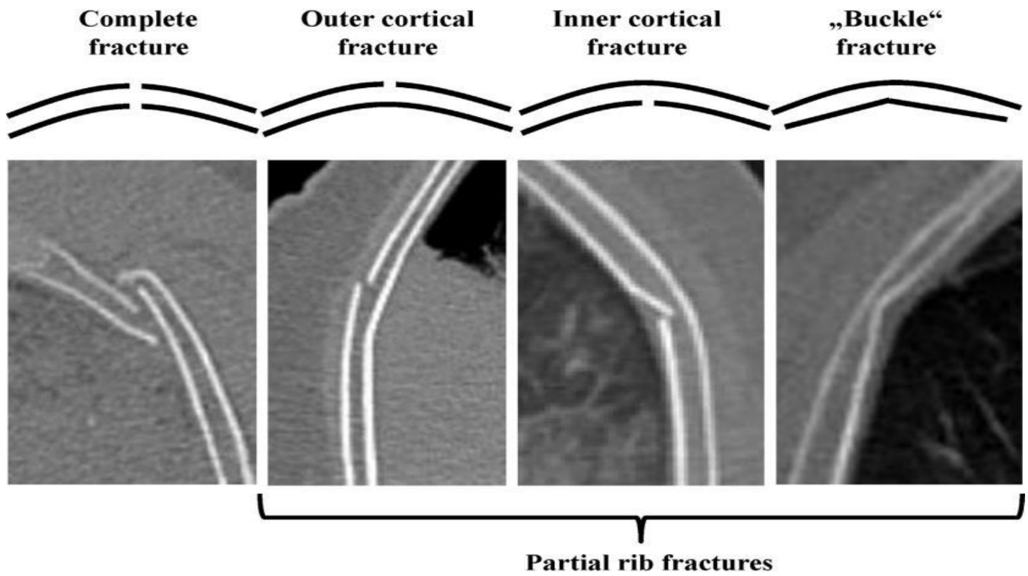


Fig 1-2. Shows different types of post-mortem rib fractures *(Schulze et al, 2014)*

Figure (1-2, Page 25) shows types of post-mortem rib fractures; a complete fracture was documented when both cortical lines were interrupted. A single dehiscence of either the outer or the inner cortical line or the formation of a sharp angle at the inner cortical line (‘‘Buckle fracture’’) were individually documented and summarised as partial fractures” (Schulze et al., 2013).

Skull fractures

Traumatic brain injury is one of the main causes of death and disability in children and adolescents and is a leading health and socioeconomic issue all over the world (Frugier et al., 2010) . This trauma necessitates a visit to the Emergency Department in the paediatric age group as acute head trauma is common (Arora et al., 2014). The estimated average number of traumatic brain injuries that occur annually among children aged 0 to 14 years is 511,257 (Faul et al., 2010). Population-based epidemiologic data has demonstrated that the highest rates of skull fracture occur in the first year of life when compared with all other groups of children (Nelson et al., 1984). Schnitzer et al. reported that 901 children aged 5 years died as a consequence of an injury or unidentified cause within the 8-year study period.

Although skull radiographs cannot identify intracranial contusion, they may be useful for discovering skull fractures. In fact, radiographs are one of the best methods to identify skull fractures in childhood (Chung et al., 2004, Arthurs et al., 2014). The sensitivity of CT to evaluate the skull fractures was as high as 85% with specificity of 100% when post-mortem findings were used as the reference standard (Chawla et al., 2015). Krentz et al. (2016) pointed out that PMCT showed less sensitivity to detect general finding compared with a conventional autopsy, but PMCT in detecting the bone abnormality was superior than autopsy in children (Krentz et al., 2016). Three-dimensional has the ability to show the different fractures that may not explain on axial images (Schweitzer et al., 2015). (Figure 1.3, Page 27) is a three-dimensional CT scan showing a skull fracture.

Infant and child injuries are a significant and growing public health problem that requires attention. Intracranial injury related to physical abuse is an important cause of morbidity and mortality in children (Wilson et al., 2014). Subdural haemorrhage is one of the main findings which is difficult to identify and presents a major challenge for the physician, courts and social workers. It is also difficult to identify in clinical practice whether a subdural haematoma in young children is caused by abuse or accident(Lonergan et al., 2003).

Fig 1-3. Shows 3D CT of the skull in an 8-year old: Shows a skull fracture

Poulsen and Simonsen, (2007) highlighted that PMCT might not identify all skull fractures, reporting that PMCT did not detect 9 skull fractures located close to the petrous part of the temporal bone and other facial fractures. The main weakness with Poulsen and Simonsen's, (2007) study is that the CT scans were reported by one forensic pathologist who had no specific training in radiology.

For this PhD, two paediatric radiologists one with 15 and the other with no previous experience of interpreting PMCT images will review the findings from PMCT and conventional radiography. Though effective in diagnosing the fractures, conventional radiographs are inaccurate at identifying intracranial injury following blunt head trauma. Due to this reason, infants routinely require CT to evaluate the brain to exclude intracranial injury (Meyer et al., 2011)

Skull radiographs, predominantly performed as part of a skeletal survey to exclude fractures that might be related to abuse, are used as the standard and most basic imaging tool for the diagnosis of skull fractures (Culotta et al., 2017).

Intra-abdominal injury

Abdominal injury is considered an important cause of death in childhood and more than 90% of these injuries have a blunt mechanism (Heron, 2015). A direct blow to or fall on to the left upper quadrant of the abdomen is the usual mechanism of a splenic injury. Recently, CT has played an important role in identifying suspected intra-abdominal injuries which are related to blunt abdominal trauma in adults (Benjamin et al., 2018). More than half of live children who were injured and presented to adult trauma centres underwent a CT scan as part of their trauma evaluation (Larson, Johnson, Schnell, Salisbury, & Forman, 2011). Recent research studies have shown that "pan" CT is superior to selective CT in adults after intra-abdominal trauma (Caputo et al., 2014). First choice to identify intra-abdominal injury is a CT scan (Streck Jr et al., 2012). A study by Beck et al. (2014) revealed that splenic and hepatic tears, pancreatic injury and duodenal hematomas can all be identified on CT scan. Their study highlighted that more research in to PMCT is required and that PMMRI should also be considered (Beck, 2014).

Recently, several studies focused on evaluating the agreement between post-mortem CT and conventional autopsy for identifying causes of death. Noda et al. (2013) prospectively compared the concordance between PMCT and autopsy. PMCT revealed an identifiable cause of death in accordance with the clinical diagnosis of death in 16/38 cases. The concordance rate with autopsy was 57% in the 4/7 who underwent an autopsy.

The study has some weaknesses however. First; the sample size (7) of subjects who underwent conventional autopsy was small. Second, the two radiologists who interpreted PMCT images were general radiologists who had no previous experience of post-mortem imaging.

1.2.1.5 Sudden unexpected death in infancy (SUDI)

For many parents, the unexpected, sudden death of a child is a particularly traumatic event (Blair, Sidebotham, Berry, Evans, & Fleming, 2006). Unexpected death of an infant is more common in babies aged between two and four months, but it can also happen to younger and older babies. It is the leading cause of death between one month and one year of age (Gould, 2001); females are less likely to die than males at a ratio of 40:60 (Moon et al., 2007). SUDI cases may have several causes of death identified but most remain unexplained and are labelled as either undetermined or sudden infant death syndrome (SIDS). Risk factors leading to DSIDS are well known including hazardous sleeping environments, parental smoking and prone sleep position, with some of these situations being caused by asphyxia (Krous et al., 2004, Fleming and Blair, 2007, Blair et al., 2006, Brixey et al., 2011) . When no explanation can be found, it is termed sudden infant death syndrome (Loughrey et al., 2000).

1.2.2 Autopsy protocol

1.2.2.1 Conventional autopsy

Post-mortem examination has different steps (1) a review of clinical history, (2) skeletal survey, (3) external examination, (4) macroscopic examination, followed by histological tissue sampling removal of the brain with the examination after fixation in 10% formalin; investigations, such as genetic and metabolic testing and virology and microbiology sampling. Routine microbiology samples obtained from cerebrospinal fluid, lung, cardiac blood, and spleen where appropriate, with more samples if needed.

1.2.2.2 Autopsy technique

1.2.2.2.1 Origins and evolution of autopsy

Herophilus's report is considered one of the oldest on dissection of the human body. He was a famous teacher in Alexandria (Greece) in 300 BC (Edelstein et al., 1967). Xavier Bichet (1771-1802) was known as the ‘father of histology’, drew the attention of the clinicians from macroscopic organs to examination of tissues during the autopsy. Xavier Bichet discovered 21 various types of tissues in the human body by different physiological and biochemical experiments; interestingly, he did not use a microscope to describe these tissues. Hospital medicine progressed rapidly during the 18th century with doctors increasingly requesting autopsies to be done to discover the cause of death. Development of the microscope led to new methods for explaining the functions of cells. Karl Rokitansky and Rudolf Virchow’s work using the microscope and the publication of Die Cellularpathologie in 1858 resulted in unprecedented progress in pathology and histological examination became a routine part of the autopsy (Edelstein et al., 1967, King and Meehan, 1973). Autopsy continued to have a significant role in the 20th century with leading clinicians spending long periods of time in the mortuary room. Good hospitals were recognised by their high autopsy rates and poor hospitals by low autopsy rates. It was generally considered that by not performing an autopsy, doctors were attempting to bury their mistakes (Edelstein et al., 1967, King and Meehan, 1973). Since 1930, pathology has developed as a clinical discipline. At that time, autopsy rates were high, but autopsies were not necessarily performed with the consent of parents. Promptly with further development of PM techniques, pathologists started branching out and sub specialising.

Autopsy has been used to identify causes of death for a long time. In an editorial in the Journal of American Medical Association (JAMA), Sir Isaac Starr questioned the value of routine autopsy (Starr 1956) and pointed out that the large volumes of information gathered in the morgue contributed little to research or clinical practice. Autopsy consent was required at that time in America, which most of the time was refused. The consent for autopsy was not required in Germany and therefore, American medical students were attending autopsies in Germany.

The defenders of the autopsy emphasise that information from an autopsy helps clinicians to identify the causes of death (King and Meehan, 1973, Edelstein et al., 1967). In 1962, the UK established the Royal College of Pathologists to maintain high standards and improve the science of pathology.

1.2.2.3 Autopsies in the 21st century

The fundamental principles of autopsy have not changed and it still has a vital role in 21st-century medicine as a means for evaluating therapies, studying new diseases and providing information to the family of the diseased. A conventional autopsy is regarded as a professional activity that requires extensive technical ability and knowledge to explain the causes of death within a wide range of clinical contexts. A medicolegal autopsy provides crucial information in identifying the causes of death and thus requires the highest possible standard of practice. Thus, clinical autopsy represents one of the situations where clinicians to discuss the detailed examination with other clinicians (Rosahn, 1956). Current guidelines in the UK (RCOG 2001; RCPCH 2002) recommend that all perinatal and paediatric deaths be offered the option of an autopsy and these examinations should be performed by specialist paediatric or perinatal pathologists. The Royal College of Pathologists specifies a minimum data set that needs to be collected in various clinical scenarios including neonatal autopsy, fetal autopsy, sudden unexpected death in infancy (SUDI) and in cases where a cardiac cause of death is suspected.

1.2.2.4 Evidence base for utility of autopsy

There is varying opinion as to whether advances in technology and availability of advanced diagnostic methods have led to a reduction in medical errors which might lead to death (Goldman et al., 1983, Landefeld et al., 1988). An accurate meta-analysis of studies with high autopsy rates has reassuringly shown a decrease in class I errors (i.e. the main findings that, if known before death, would have changed clinical management potentially resulting in prolonged survival or a cure) detected within post-mortem examination in the last 4 decades (relative risk decrease of 33.4% per decade (95% CI–8.4%-51.6%) (Shojania et al., 2003)**.** In spite of this decrease, class I errors continue to be reported in 8.5% to 12% and class II errors (i.e. the main findings that, if known before death, would have changed clinical management because the treatment was being given already or was not available) in 13.6% to 29% of neonatal babies or PM of children (Stambouly et al., 1993). In a review of 27 studies, the perinatal PM examination resulted in a “change in diagnosis” or “additional findings” which might have affected management or counselling in 22 (76%) cases (Gordijn et al., 2002), the rate varying between 22-49% for terminations of pregnancy and 28-75% for stillbirths.

1.2.2.5 Factors influencing the yield from autopsy

There are several factors which might affect the usefulness of conventional autopsies such as the sophistication of ante mortem imaging, the antenatal diagnostic approach and also, the level of clinical expertise might reduce the likelihood of discovering additional findings at PM (Goldman et al., 1983, Landefeld et al., 1988). Gordijn et al. mentioned that the experience of the pathologist to identify the cause of death is very important, where specialist perinatal/ paediatric pathologists in tertiary centres have the ability to identify useful information (Gordijn et al., 2002, Gordijn et al., 2007). During the process of autopsy, the specialist pathologist removes and fixes the brain before dissection; a process which takes around 3 weeks. However, parents of the deceased stated that all organs of the body must be returned to the body before burial. Adequate fixation is hard to achieve within this timescale. A delay between intrauterine death and delivery will lead to maceration that can make examination of the brain more difficult for the pathologist. The requirement for consent for autopsy may reduce the availability of information about abnormality in the foetus’s' body (Rose et al., 2006).

1.2.2.6 Components of the post-mortem examination

PM examination is a complex process and includes careful integration and analysis of information drawn from different sources, including ante-mortem investigation, detailed external and internal examination of the corpse and a wide range of microbiological, cytogenetic, histological and immunohistochemical investigations.

1.2.2.7 Non-invasive and minimally invasive components

1.2.2.7.1 External and Macroscopic Examination

That includes careful review of the medical history of the patient and investigations before death to explain the causes of death. Basic measurements, including head circumference, crown-rump length, crown-heel length and foot length, are taken from the dead body and compared to measurements in standard reference tables. These measurements from fetuses will allow the estimation of intrauterine fetal growth. Evaluation of the degree of maceration or post-mortem change includes documenting the extent of skin discolouration, blistering and skin slippage, and allows the pathologist to estimate the duration of time since death, although such estimates might not be precise. Special emphasis is placed on distinguishing possible dysmorphic features which, despite the external appearances, should be interpreted in the context of the gestational age and subtle syndromic abnormalities might not be readily discernable in mid-trimester fetuses. This is useful when subsequent reviews are required, for example, by a geneticist (Keeling, 2013).

1.2.2.7.1.1 Other additional investigations

Microbiological and biological analyses, as well as metabolic studies (blood and enzyme assays using cultured fibroblasts harvested from a post-mortem skin biopsy or bile spots for acylcarnitine profiling by tandem mass spectrometry), and cytogenetic and DNA analysis are also considered important for identifying the causes of death as part of the PM examination.

1.2.2.7.2 Dissection and Direct Internal Examination of Visceral Organs

The information from the macroscopic investigation of the visceral organs is complementary and considered as an important part of the autopsy examination. A traditional autopsy is usually performed to examine the chest, pelvic and abdomen organs via a midline incision through the anterior thorax and abdomen. A careful observation of the internal organs is performed prior to their removal for measuring, weighing and dissection. Photographs are taken of organs which potentially show abnormalities and small samples are taken for histological examination. Finally, all organs must be returned to the victim's body (Department of Health and Social Care, 2018). All these organs are routinely weighed and compared with reference tables. The most useful weights are those of the brain and liver for identifying fetal intrauterine growth. When aimed to check brain tissue, the scalp is incised posteriorly, either by means of a coronal incision or vertical midline incision from the top of head to the occiput. Also, the skull is always opened by following the non-fused cranial suture lines, though in older infants cranial bones may be difficult to cut. In addition, the brain is always examined following a period of 10% formalin fixation, which may need several weeks to investigate complex brain anomalies. Reagents for rapid fixation of the brain that decrease the period of brain retention to a few days instead of weeks have recently become available. Examination of skeletal abnormalities and injuries require comprehensive dissection of the whole body (Malcomson and Keeling, 2007).

1.2.2.7.3 Microscopic Examination

Taking small samples of tissue from organs is important in post-mortem examination to exclude or confirm the presence of diseases. In more than 25% of pediatric PM examinations, the final decision is made based on histological results. Histological examination of lungs tissue for pneumonia and myocarditis are very important (Weber et al., 2008a, Weber et al., 2008b).

Neuropathological examination has critical importance in improving the current understanding about a wide range of degenerative and developmental diseases. This is less important in cases of fetuses terminated for malformations, especially of the brain tissue, which are almost always of a structural cause. Histological examination of internal tissues might provide little extra diagnostic information except for specific organs such as the lungs, liver and kidneys , where renal diseases can be associated with syndromic defects (Corabian et al., 2007).

1.2.2.7.4 The post-mortem report

Recent guidelines recommend that a first report is provided to the clinician within two days of the PM examination, followed by a final report which should include final results of the histological examination and results of other investigations (The National Sentinel Caesarean Section Audit Report, 2001), which should be provided within four to six weeks of the PM examination. The PM report should document macroscopic and microscopic results, as well as include the results of all investigations performed. Photographs of histological or macroscopic abnormalities and X-ray images should be included in the PM report. The PM pathologist should discuss the contents of the PM report with parents and a decision made regarding whether a copy of the report should be given to parents. Some parents may find the technical jargon (and photographs) used in such reports distressing (Keeling, 2013, Nicholl et al., 2007).

1.2.2.8 Human tissue act (HTA) and consent for autopsy

The human tissue act (HTA) is regulatory body which provides legal advice and guidance and was responsible for defining a minimum set of standards published as codes of practice (see http://www.hta.gov.uk). Consent is necessary in the case of the removal, storage and use of human tissues for autopsy for (a) determining the cause of death; (b) obtaining scientific or (c) medical information that may be relevant to any other body in the future; screening; research in connection with disorders of the human body; implantation; clinical scrutiny. Education or training on human health; evaluation of performance; monitoring of public health; and quality assurance.

This applies to all human tissue removed at PM examination, including small samples such as blocks and slides and samples that may be kept as part of the medical record. The Act (Code of Practice HTA 1) provides for approval as a positive measure; lack of parental refusal for a PM examination is not sufficient evidence of consent. Valid consent should be given voluntarily by an appropriately informed individual who has the ability to approve the activity in question such as a parent. However, if there is disagreement between the parents, it should be discussed sensitively with both parents before proceeding to a post-mortem examination. It is important that consent should not be viewed as single act, for example, the signing of a consent form, but rather that it should be seen as an ongoing process in which parents can discuss the full issue, ask questions and make suitable choices Seeking consent is usually the responsibility of the clinician, who should have knowledge of the PM examination procedure.

1.2.2.8.1 Audit, quality control and teaching

The post-mortem examination plays an important role in auditing.

1.2.2.8.1.1 Medico Legal Issues / Malpractice Litigation

Frequently, the pathologist is requested to perform a coronial autopsy if there is any risk of the case relating to post-operative death or an intrapartum event. In these cases, questions usually relate to the timing of events, such as the timing of hypoxic-ischaemic brain injury, presence of iatrogenic injury, or meconium staining, and placement of long lines or other therapeutic interventions.

1.2.2.8.1.2 Epidemiology

Autopsy is used as a way of collecting epidemiological data. This is especially important as new diseases and epidemics emerge. Nevertheless, the accuracy and utility of such a procedure at an individual level is questionable (Gordijn et al., 2002, Gordijn et al., 2007)

1.2.2.9 Post-mortem imaging

Skeletal survey examination is performed in all children below 1 year of age and any older children in suspicious circumstances of or unexpected death. The finding of the skeletal survey is undertaken and reported by a specialist radiologist prior to PM examination. Skeletal survey and autopsy examinations are complementary especially in suspicious cases, and the skeletal survey may be more useful than autopsy for identifying fractures. Alternatively, PM examination might detect some fractures (for instance fresh rib fractures), which may not appear on the skeletal survey. PMCT is increasingly being used, particularly in adults, to examine the skeletal system (Malcomson and Keeling, 2007).

1.2.3 Acceptability of Post-Mortem Imaging among Muslim and non-Muslim Communities

In the forensic field, post-mortem examination is one of the important steps to explain the circumstances of death. However, autopsy rates across the whole world have declined due to different reasons, including religious beliefs and legal considerations (Gulczyński, Iżycka-Świeszewska, & Grzybiak, 2009).

1.2.3.1 Brief description of Islam, beliefs, and sources

The Islamic religion, which began in 610 A.D., is considered the second largest religion with more than one billion Muslims worldwide (Rispler-Chaim, 1993).

All Muslims have the same concepts, but may differ on some jurisprudential issues, particularly those that are not explained clearly in the Koran or Hadith. Furthermore, Muslims live in many places around the world, and Islamic law is only applied in Muslim-ruled countries (approximately 40 countries) and some laws formulated by humans, which are used to guide the people in all the countries in the world (Payne-

James et al., 2003). Muslims also believe that post-mortem examination is not necessary because death occurred according to the will of God (Al-Adnani and Scheimberg, 2006). Most religions have concerns about the performance of autopsies, but, in the opinion of the researcher, Islam has the greatest reservations. Islam, based on the Hadith, calls for respect for the body and recommends that the body should not be disfigured; “The breaking of the bone of a dead person is like breaking the bone of a live person” (Davis and Peterson, 1996). It states that the body be buried promptly after death and that there be no cremation of the body (Oluwasola et al., 2009). In some countries, the duration of consolation lasts for three days after the burial and Muslims bury the body as soon as possible after death. (Midelfart J, 1998).

In a study conducted in Zambia by Lishimpi et al. (2001), 891 out of 1603 (56%) parents refused to give permission for autopsy due to beliefs that the autopsy wasted time and would not benefit them. Muslim participants (3.4%) refused to consent for autopsy due to their beliefs and preferred to burial the body within 24 hours after death. In addition, 43% of participants were angry that the autopsy had been requested and felt that the diagnosis should have been identified when the child was alive. The participants also showed concern for other reasons: unwillingness to postpone the time of burial once the death certificate had been issued and because arrangements for the transfer of the body had already been made (Lishim et al., 2001). The relatively low proportion of Muslims who refused autopsies in their study may have to do with the number of Muslims in Zambia. Al-Saif et al. (2016) found that 21% (390/1866) of their participants refused autopsy for religious reasons and 72% (1350/1866) believed that the autopsy should not be done without having consent from the parents or guardians of the deceased.

Rankin et al. (2001) distributed 258 questionnaires to women who lost their babies and attended a bereavement counselling service. For a variety of different reasons, 81% of those mothers agreed to an autopsy examination. The main reasons were that mothers wanted more information about the cause of death (44%) and wanted to contribute to improving medical research (24%). Twenty-eight mothers did not give their consent for an autopsy examination because they felt they did not need more suffering by consenting to an autopsy. Thirteen mothers felt the autopsy would not help to explain the cause of death (Rankin et al., 2002). The study specifically selected a sample of mothers and aimed to evaluate the acceptance of autopsy examination from them after losing a baby during pregnancy or in the neonatal period. The researchers thought that this loss might affect the family less than losing a child or adult.

But the author did not mention the religion of the participating mothers, which might affect their opinions.

Maintaining the dignity of the body is important to all families and relatives. PMMRI and PMCT are less invasive (virtopsy) and are not associated with the risk of tissue devastation or other artifacts that are produced through the process of tissue sampling for histological examination (Thayyil et al., 2009a). Unenhanced PMCT can be useful primarily for identifying abnormalities of the bone and air spaces, for guiding the conventional autopsy examination, and as a paramount tool in non-criminal cases where there is no consent from the relatives to perform an autopsy (Woźniak et al., 2015). PMCT showed the same causes of death in 67% of child cases when compared with conventional autopsy (Sieswerda-Hoogendoorn et al., 2014). In the case of supposed natural unexpected death, a thorough post-mortem evaluation, including post-mortem imaging, is offered to the parents of the deceased child (Sarikouch et al., 2008).

Cannie et al in a 2012 study, compared the acceptability of conventional PM autopsy with virtopsy (PMMRI) and evaluated the reliability of PMMRI in identifying the structural abnormalities of fetuses. The study showed that 70% of non-Muslim mothers accepted a classical autopsy of their child's body compared with just 40% of Muslim mothers (Cannie et al., 2012); however, only a relatively small number of cases where involved in the study. In addition, the study specifically selected a sample of women to consent to a form of non-invasive post-mortem such as PMMRI and/or PMCT, which may introduce bias into this study.

Ben-Sassi et al. (2013) evaluated the acceptance by healthcare professionals of less invasive autopsy compared to standard autopsy. The study found that autopsy was perceived more favourably, with certain demographic factors affecting the overall conventional autopsy acceptability, including ethnicity (more Caucasian and African individuals preferred autopsy compared to Arabic, Indian and Asians), and religion (people with no religion and Christians found PM examination more acceptable than those of Sikh or Islamic faiths). Less invasive autopsy was more acceptable compared to autopsy (9 vs 8); 49.6% found less invasive autopsy and conventional autopsy equally acceptable, 39.7% found less invasive autopsy more acceptable than conventional autopsy and 10.7% regarded less invasive autopsy as acceptable (this was due to concerns about the inaccuracy of post-mortem medical imaging) (Ben-Sasi et al., 2013).

Participants in the Ben-Sassi study shown that medical and non-medical parents had different opinions, as a result of their professions. Ben-Sassi’s study highlighted that further research is needed with regards to this topic.

1.2.4 Estimating duration of death

The time since death is known as the post-mortem interval (PMI), and estimating this is one of the essential tasks of the forensic pathologist who is consulted when a dead body is found. Other important tasks include verification of the identity of the victim, recording the injury patterns and identification of the weapon used in the crime. One of the goals of criminal law is a precise estimation of the post-mortem interval, as this enables verification of witness statements, thus limiting the number of suspects involved. Incorrect estimates of the time of death can lead to confusion and complications with investigations (Kaliszan et al., 2009). Between 1984 and 2015, Chinese forensic scholars made great progress in improving the estimation of the date of death. Several methods have been used and these can be divided into the following categories; spectroscopic technology (Fourier transform infrared or Raman micro spectroscopy); entomological methods (either a carrion insect development or a succession model) or molecular biology methods (degradation of DNA, RNA or proteins).

1.2.4.1 Stages of post-mortem change

As duration of death proceeds, there are several early changes in the cadaver that result in specific changes in the physical nature and/or appearance of the body prior to the onset of gross, recognisable decomposition. Post-mortem changes have been used to estimate the PMI and the stages of decomposition should be determined (Lee Goff, 2009). These changes are described below.

1.2.4.2 Livor mortis

Livor mortis is one of the early changes observable after death and is a physical process. The main function of the heart is to circulate the blood around the body. After death, the circulation stops and the blood begins to settle, by gravity, to the lower regions of the body. This leads to discoloration of the lower limbs. Although beginning immediately, the first signs of livor mortis are typically observed after a period of about 1 hour after death with full development being observed 2–4 hours after death. The blood is still liquid at this time and pressing on the skin will result in the blood being squeezed out of the area (blanching), only to return once pressure is removed. After 9–12 hours following death, the pattern will no longer change, and the livor mortis will be 'fixed.' Any areas of pressure resulting from continued pressure or clothing pressure during this period will not show discoloration (Nashelksy and McFelley, 2003).

1.2.4.3 Rigor mortis

This chemical change leads to post-mortem stiffening in the muscles due to changes in the myofribrils. Immediately after death, the body is easy to flex. The first observation of rigor occurs between 2-6 hours following death and then develops further over the next 12 hours. Rigor mortis begins with the muscles of the face and then develops in all of the muscles of the body within the first 4-6 hours. The period of rigor typically continues for 24-84 hours, after which the muscles begin to relax again. The onset and duration of rigor mortis are dominated by two primary factors; the metabolic state of the body and the body temperature. Lower ambient temperatures can accelerate the onset of rigor and prolong its duration, while the opposite is found in warmer temperatures. If the body has been involved in vigorous activity immediately before death, the onset of rigor is more rapid. Rates of cooling after death and body mass also effect the onset and duration of rigor mortis (Gill-King, 1997).

1.2.4.4 Algor mortis

After death, the body stops regulating temperature and the internal temperature begins to approach the ambient temperature. In most instances, this includes a cooling of the body temperature until ambient temperature is reached, usually in a period of 18–20 hours (Gill-King, 1997).

Recording post-mortem changes of the body is an important method for estimating the time of death. Putrefaction naturally occurs after death (Fenoglio, Bo, Cammarata, Malacarne, & Del Frate, 2010, Powers, 2005) and the process of putrefaction begins with autolysis (Vass, 2001). Self-liberated enzymes are directly related to self-degradation (Tsokos, 2007, Knight, 2004). Vass (2001) provides a good preliminary explanation of the processes leading to automatic disintegration; when oxygen levels in the cells have become depleted, carbon dioxide increases as a natural metabolite produced by cellular processes and this briefly lasts in some cells after death. As a result of this increase in carbon dioxide, the pH of the body's tissues becomes acidic, and natural detoxification processes stop. Waste products such as lactic acid then start to increase. The cell membranes are not maintained after death as in the life-period and levels of adenosine triphosphate decrease due to loss of membrane structure. Moreover, due to the rising adenosine triphosphate levels, transport within cellular membranes is unregulated and the cell might begin to swell (Gill-King, 1997). Furthermore, some of the enzymes, naturally found compartmentalised in the body, which are responsible for dissolving the cell membranes, cause destruction and the release of fluid cellular contents into the body. Self-decomposition first becomes apparent in areas of the body with higher levels of metabolism (Gill-King, 1997, Vass, 2001). At the beginning of this process, decomposition will be inside the cell and not visible to the naked eye. Changes occur slowly and increase until post-mortem changes occur. This process will continue in the decomposition of the bone tissue, which, as previously discussed, takes a long time. This is very important when understanding post-mortem changes and is crucial for estimating the post-mortem interval (Fenoglio et al., 2010).

There are several factors that may affect the rate of decomposition at which occurs in the body. The size of the body is the main factor; a small body will cool faster than a large body in the same ambient temperature. Exposure to sunlight or heating may also affect the rate of cooling as may clothing. The commonly used temperature in these calculations is from the liver although rectal temperature may also be used (Nashelksy and McFelley, 2003). However, when the body is in an advanced state of decomposition, the enormous variability in the rate of putrefaction and post-mortem change complicates estimation of the time of death (Cardoso et al., 2010).

The decomposition mechanism is a transformative and devastating phenomenon consisting fundamentally of the degradation and putrefaction of organic matter by anaerobic bacteria, mostly habitual saprophytic hosts of the intestine and aerobic bacteria which are mostly airborne (Spitz and Fisher, 1980, Perper, 1993). Microbial factors play a more important and aggressive role in decomposition than tissue autolysis (Campobasso et al., 2001). The putrefaction of corpses is a mixture of different processes ranging from autolysis of individual cells by internal chemical breakdown, external processes introduced by bacteria and fungi from both the intestine and outer environment, to tissue autolysis from liberated enzymes (Coe, 1993). Despite several decades of investigation on the topic of estimating time of death, accuracy in defining the time of death has not significantly improved, and no single method can be reliably used to accurately estimate the PMI (Brooks, 2016).

In forensic medicine, measuring the temperature of the victim is very important when using post-mortem changes in the body for determining the time of death (Brinkmann et al., 1976, Henssge and Madea, 2004). Al-Alousi et al (2002), when studying 117 cases under controlled conditions, used a cooling system to focus on the shape of the post-mortem cooling curve. These cases were divided into two groups; naked or covered body. The torso was covered with two blankets, but not the head in the latter group. The rectal cases were divided into the naked body groups (70 cases) and into fat and thin categories depending on the value of the ‘‘cooling size factor (Z)’’. The body was considered thin if Z was > 0.028. The brain, liver, rectum and the environmental temperatures for each case were continuously monitored soon after death and for up to several hours after death. The study found that the cooling curves for the three body areas were a combination of shapes and the slopes of the curves varied throughout the controlled period. The ‘‘initial temperature plateau’’ was found on average in 22% of all cooling curves with the plateau incidence being significantly higher in the rectal curves (27% of rectal curves compared with 7% of brain and liver curves, P < 0:1%) (Al-Alousi, 2002). However, this method may require direct contact with the body, which may be difficult due to decomposition.

Gulyás et al. (2006) focused on measuring the superficial brain temperatures (4cm and 8cm deep) in 8 cases. The measurements were taken serially every 1 min (in 4 bodies) and every 5 min (in the other 4 bodies). These measurements were started at the moment of death at 121 min after death and continued for between 11 and 21 h. The study stated that the relationship between ‘‘post mortem temperature and biochemical parameters’’ can be replaced with a ‘‘post mortem time—biochemical parameter’’ relationship. However measuring the temperature of deep brain tissue (Gulyás et al., 2006), is an invasive process.

Henssge et al. (2004) stated that there are a large number of research studies on ‘‘estimating the time since death’’ that only described the time-dependent parameters. However, research to provide new methods for analysing post-mortem parameters is not effective since almost all parameters change (to some degree) with rising post-mortem interval. Using new techniques (Sabucedo and Furton, 2003) has not led to improvements in the estimation of time of death (Madea, 2005).

Janjua et al. (2008) placed 25 pig femora and 25 metatarsals studs outdoors for more than 291 days for observation to establish: (1) orthopaedic patterns for estimating time since death in southern Ontario; and (2) whether larger (femora) or smaller (metatarsals) bones provide a better indicator of time since death. Different factors affect the breakdown of bone, such as ambient air temperature, humidity, precipitation, sunlight, soil pH, and freezing and thawing. In addition, climatic conditions increased the decomposition of soft tissue. Janjua's study stated that both soft tissue and bone decomposition was affected by an animal activist, that lead to variability in sample bone decay and decomposition. The difference in the microenvironment, partly caused by introduced variability and soil composition, affected bone weathering rates. Four stages of orthopaedic orthosis were established based on observed patterns. Femora proved to be more flexible and showed higher degrees of change due to weathering, which indicates that it would be a better indicator of time since death than smaller metatarsal bones. (Janjua & Rogers, 2008). This method might provide useful information if the victim is found a long time after death. However, this method still has risks such as the transmission of some diseases and also may take more time to get results. In addition, it is a difficult technique to use when the cadaver is in an advanced state of decomposition and estimating the date of death is more complicated. In this situation, estimating the time of death using CT scan might be an easier and faster method.

A forensic process defining PMI fundamentally relies upon the body post-mortem changes, such as body temperature, rigor mortis, livor mortis, vitreous humor changes, in association with autopsy findings; for example, the temperature of contents, which digested in the stomach, the amount of urine in the bladder, as well as the expertise of the forensic doctor. All of these factors can have an effect on determining post-mortem interval. Whilst an autopsy is an important process to determine the cause of death, the traditional autopsy takes a long time to complete. In addition, Thayyil et al (2013) it is an invasive procedure and the expertise required and other factors such as religion and culture (relating to maintaining the dignity of the body) lead to very low autopsy rates worldwide (Wang et al., 2017).

Recently, computed tomography (CT), magnetic resonance imaging (MRI), and other imaging techniques have become important methods for post-mortem examination (Thali et al., 2004). Medical imaging was developed well before the 1990s opened up new perspectives on the use of CT and MRI and it has been used as part of the autopsy process (Donchin et al., 1994). Several studies have begun using CT and/or MRI and 3-D surface surveying as a less invasive way to objectively identify internal and external body injuries and fractures in PM cases (Thali et al., 2005). Forensics have used medical imaging to help diagnose causes of death.

Measurement of Hounsfield unit (HU) is a capability of CT scans. The HU is defined as attenuation of the CT x-ray beam and depends on the thickness of the anatomy traversed and the composition (physical density and atomic number) of the tissues in the path of the beam. After image reconstruction, each pixel in the CT image is assigned a number, referred to as a CT number, which is a rescaled normalised function of the linear attenuation coefficient. These scales are calibrated such that the HU value for water is 0 and for air is -1000 at all tube energies used (Bushberg and Boone, 2011, Lamba et al., 2014).

Recently, Wang et al. used PMCT to evaluate changes in different organs in adult rabbits using the HU. Their study suggested that analyses of several indicators from different organs might make the study of PMI estimation more scientific and enhance operability in the future.

1.2.5 Conclusion

Conventional autopsy is the accepted gold standard for identifying the causes of death, but it is associated with several issues and in recent years its use has been declining worldwide as a result of religious, cultural and emotional factors. PM imaging may be more acceptable and reduce negative emotional impacts on parents. This study aims to ascertain the opinions and preferences of Muslims and non-Muslims regarding PM imaging (PMCT and PMMRI), through distributed questionnaires to Muslims in Libya and Muslims and non-Muslims in the UK. Post-mortem imaging for forensic examination (including for sudden unexpected death in infancy) is being increasingly used and can provide a range of helpful information. It also has other benefits, for example, corpses can be scanned quickly, even inside a body bag. This study will explore the usefulness of PMCT in the determination of cause of death in infants and children. The results may support the use of PMCT as an alternative to conventional autopsy; or if not, to what extent it can be used as an adjunct to conventional autopsy. Determined the time of death is one of the essential tasks of the forensic pathologist who is consulted when the dead body is found. Previous study highlighted that analyses of several indicators from different organs might make the study of PMI estimation more scientific and enhance operability in the future. This study will use assess the ability of total body air volume and HU to non-invasively estimate PMI.

2. Chapter Two

2.1 Acceptability of Post-Mortem Imaging among Muslim and non-Muslim Communities

https://doi.org/10.1259/bjr.20180295

2.1.1 Abstract

Objectives:

People's reactions towards autopsy vary according to their cultural and religious beliefs. This paper aims to determine the reaction towards this procedure among Muslims resident in Libya, Muslims and non-Muslims resident in the UK.

Methods:

320 questionnaires were collected from the three communities, interrogating belief about post-mortem investigations and after what type of death these were appropriate. Descriptive statistics and non-parametric statistics were used to analyse the data.

Results:

All groups felt that children should be buried sooner than adults ($p<0.001$) but 73% of Libyan Muslims thought that children should be buried within 12 hours of death ($p < 0.001$). Type of death altered what sort of investigations were desired. In the case of homicide, Libyan Muslims were less likely to prefer CT ($p<0.001$) or MRI ($p=0.001$). Both Libyan and UK Muslims wanted autopsy for homicide (Libya: $p<0.001$, UK: $p=0.022$) and did not want autopsy in the case of expected death (Libya: $p<0.001$, UK: $p<0.001$). Non-Muslims prefer to use autopsy in case of unexplained ($p<0.001$) or expected death ($p<0.001$). All groups thought that autopsy delayed burial ($p<0.001$), did not maintain the dignity of the body ($p<0.001$) and placed an emotional burden on relatives ($p<0.001$).

Conclusion:

Post-mortem imaging is acceptable to both Muslims and non-Muslims in Libya and the UK. Muslims have a significant preference for post-mortem imaging compared to autopsy except in homicidal cases.

Advances in knowledge:

This study showed that participants preferred less invasive methods over an autopsy, but the Muslim preferred an autopsy for the investigation of homicides.

2.2 Introduction

Autopsy is regarded as the gold standard for identifying cause of death (Underwood, 2012). Clinically important information is discovered in up to 46% of neonatal and infant autopsies and the procedure is important for eliminating abuse as a cause of death (Thayyil et al., 2010). In the last three decades, however, autopsy rates across the world have declined by 40-50% (Stawicki et al., 2008). This decline has been influenced by religious, cultural and emotional factors (Noda et al., 2013). Furthermore, fewer parents are willing to consent and fewer clinicians are asking for permission to perform the autopsy (Thayyil et al., 2010, Sieswerda-Hoogendoorn and van Rijn, 2010). Other reasons given for this decline include administrative bottlenecks when requesting an autopsy and delays in providing the autopsy report (Oluwasola et al., 2009).

Muslims teach that Allah stressed the importance of maintaining the dignity of the body before and after death. Islam, therefore, calls for respect for the body and recommends that the body should not be disfigured, based on the Hadith, “The breaking of the bone of a dead person is like breaking the bone of a live person” (Mohammed and Kharoshah, 2014). Furthermore, Islam requires that the body be buried soon after death, and that there be no cremation (Lishimpi et al., 2001). An Islamic fatwa (opinion), issued in 1982, however, states that the benefits of autopsy may be greater than its disadvantages, if it serves justice (Puranik et al., 2014).

Over the last three decades, post-mortem imaging has been increasingly used as part of the forensic examination and provides significant information. Post-mortem computed tomography (PMCT) or magnetic resonance imaging (PMMRI) scans can be used to detect some causes of death as an addition to, or instead of, a conventional autopsy (Underwood, 2012). Medical imaging is particularly useful when consent for conventional autopsy has been withheld. PMCT offers a rapid method of scanning the whole body (including inside a body bag) (Thayyil et al., 2010) and is now widely used in forensic medicine in adults.

Currently, however, neither MRI nor CT are suitable replacements for an autopsy for children in all circumstances. In recent studies of PMCT, misinterpretation of PM change and/or poor imaging have led to the cause of death being misdiagnosed (Hussain et al., 2006, Oyake et al., 2006). Caution and the development of expertise in interpretation are therefore required. In their study, Sieswerda-Hoogendoorn and van Rijn (2010) state that CT identifies bone fractures more reliably than autopsy, including sites such as the face, which might be overlooked during an autopsy examination (Stawicki et al., 2008). MRI has been shown to be more acceptable to some parents than conventional autopsy for identifying the cause of death of their child (Cannie et al., 2012, Wichmann et al., 2012). Recently, some UK healthcare centres have begun issuing death certificates which include reports of PMMRI findings that are accepted as medico legal documents (Thayyil, 2010).

PM imaging has the advantages of being non-invasive and less time consuming than conventional autopsy. Data storage offers the chance to review cases in later years and the ability to highlight areas of interest before (and thereby guiding) the forensic pathology investigation (Underwood, 2012). Despite these advantages, conventional autopsy is still the only modality available in Libya for both children and adults. A search of the literature in PubMed, Medline and the Cochrane Systematic Review databases was conducted to identify studies related to the opinion of Muslims on the use of PM imaging to diagnose cause of death; no relevant publications were identified. Prior to the (potentially widespread) introduction of PM imaging to Libya, we aimed to ascertain the opinions and preferences of Muslims and non-Muslims regarding PM imaging (PMCT and PMMRI).

2.3 Methods

2.3.1 Study Design

This study used a non-validated questionnaire (Figure 1) divided into three sections, the first being related to respondents' demographics. The second section addressed respondents' knowledge of PM examinations (autopsy, CT and MRI). The third and final section explored reasons why PM examinations might be unacceptable to respondents. A total of 400 questionnaires were distributed to adult volunteers as follows: Group 1: 75 Muslim adults attending an out-patient clinic at Assafwa International Hospital, which is one of the main hospitals in the central region of Libya and 75 Muslim students and teaching staff at Misurata University in Libya. The completed questionnaires were distributed and collected by a colleague in Libya, who then scanned and emailed them to MBT; Group 2: 50 Muslim Libyans self-selected from those attending a regular monthly Libyan community meeting in Sheffield, UK. Participants in Group 2 returned their completed questionnaires to MBT at the Libyan community centre; Group 3: 200 non-Muslims (110 distributed to members of a community centre in Sheffield and 90 to staff and students at the University of Sheffield). Participants in Group 3 also returned their completed questionnaires directly to MBT. The questionnaire was in Arabic for all respondents in Libya and in English for respondents who were resident in the UK.

2.3.2 Ethical approval and consent process

Distributed with the questionnaire was a participant information sheet detailing the nature of the research, the rules governing research and the research objectives, assuring participants that their anonymity would be protected and that responses would be treated with the utmost confidentiality and used only for the purposes of this project. The information sheet also gave a short background to traditional autopsy, CT and MRI. Return of the completed questionnaire was taken as informed consent. The above process was granted ethical approval by the University of Sheffield (Reference Number 007234). Separate ethical approval was also obtained from Misurata University in Libya.

2.3.2.1 Statistical Analysis

Descriptive statistics summarise respondents' demographics and non-parametric tests were used to compare between groups and methods of investigation. Comparison between groups was by the chi-squared test. Monte-Carlo significances were calculated rather than the traditional asymptotic analysis approach. For age, a Kruskal-Wallis test was used and a Mann-Whitney for sex. Cochrane-W was used to compare the differences between the different investigations. Statistical analyses were performed using the Statistical Package for the Social Sciences, version 24 (IBM, Armonk NY). Statistical significance was set at $p < 0.05$.

2.4 Results

Of the 400 distributed questionnaires, there was a high return rate of 320 (80%) (Table 2-1, Page 58 & Figure 2-1, Page 59).

Table 2-1. Respondents' demographics Group 1 = Muslims in Libya Group 2 = Muslims in UK Group 3 = Non-Muslims in UK

Analysis Groups *									
Religion		**Group 1**		**Group 2**		**Group 3**		**Total**	
Age	**<= 25**	43	31%	0	0%	63	46%	106	33%
	26 - 30	35	25%	6	13%	28	20%	69	22%
	31 - 40	24	17%	21	47%	21	15%	66	21%
	41 - 65	34	25%	18	40%	23	17%	75	23%
	66+	2	1%	0	0%	2	2%	4	1%
Sex	**Male**	88	64%	31	69%	73	53%	192	60%
	Female	50	36%	14	31%	64	47%	128	40%
Ethnicity	**Mixed**	138	100.0%	45	100.0%	1	1%	184	58%
	White	0	0%	0	0%	86	63%	86	27%
	African	0	0%	0	0%	18	13%	18	6%
	Black	0	0%	0	0%	7	5%	7	2%
	Asian	0	0%	0	0%	24	18%	24	8%
	Other	0	0%	0	0%	1	1%	1	0%
Income	**Less than £250**	30	2%	4	9%	1	1%	35	11%
	£250 - 500	14	10%	2	4%	0	0%	16	5%
	£500 - 750	30	22%	4	9%	16	12%	50	16%
	£750 - 1000	45	33%	11	24%	37	27%	93	29%
	£1000 - 2000	15	11%	14	31%	16	12%	45	14%
	£2000 - 3000	2	1%	5	11%	48	35%	55	17%
	More than £ 3000	2	1%	5	11%	19	14%	26	8%

a Group 1, Muslims in Libya; Group 2, UK Muslims; Group 3, UK non-Muslims.

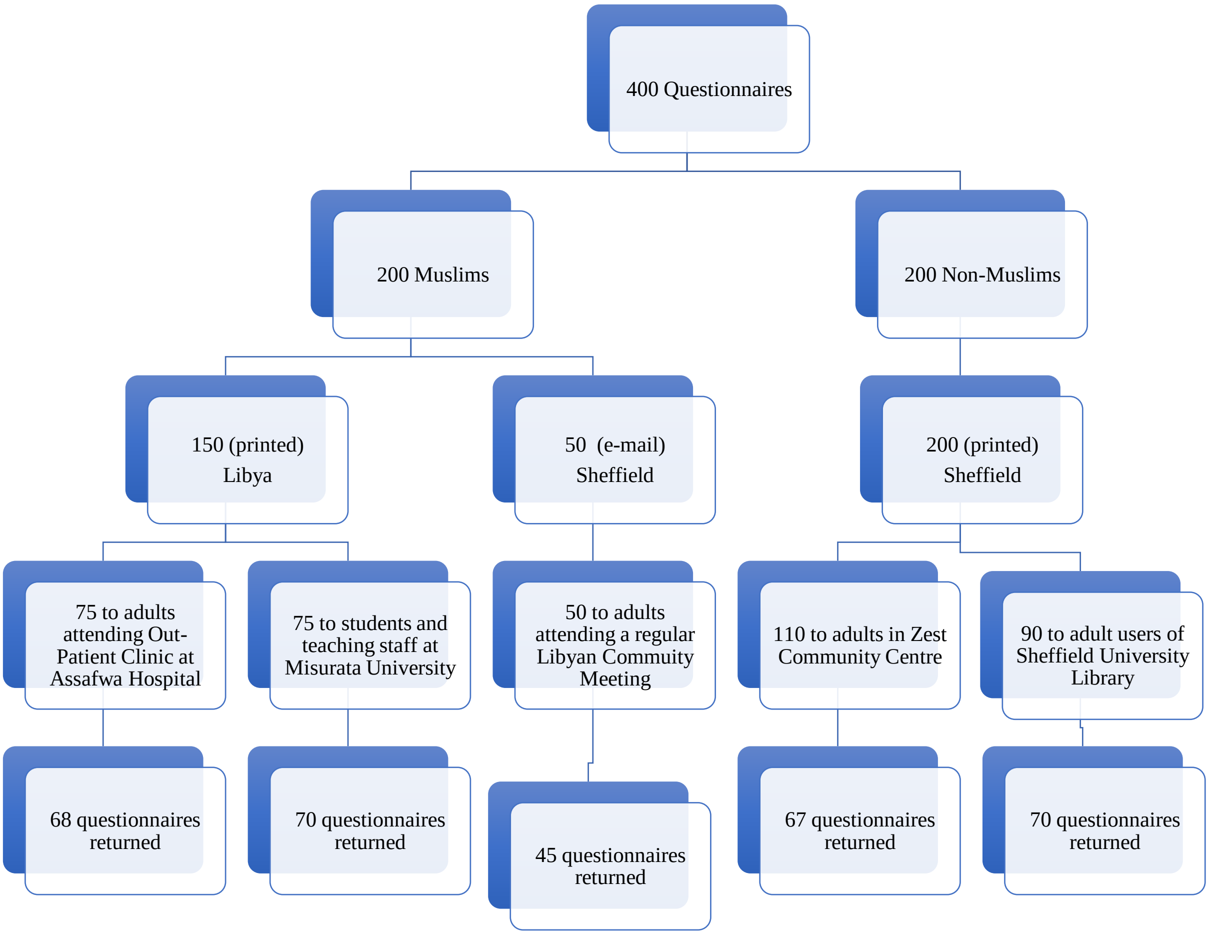


Figure 2-1. Distribution of questionnaires/response rate. The figure summarises distribution of the questionnaire and response rate from the various groups of respondents

There was a significant difference in the age of the three groups (KW= $p<0.01$) with median (90% CI) for Groups 1, 2 and 3 being 30 (27-32), 38 (35-41) and 27 (24-28) years respectively. Equally there was a significant relationship between education level and the three analysis groups ($p=0.004$) with 91.1% of UK Muslims having higher education; however, as there was very little evidence of a separate education effect, this was ignored in the further analyses.

Asked whether they had previously heard about post-mortem imaging, the percentage of positive responses for PMCT and PMMRI respectively were Group 1: 16% and 14%, Group 2: 7% and 6% and Group 3: 31% and 80% ($p<0.001$).

For both adult and child burials, differences in opinion concerning an acceptable delay in burial were significant when comparing the three respondent groups and when comparing all Muslims to non-Muslims (p ranged from <0.001 to < 0.011, Table 2.2, Page 60).

Table 2-2. Acceptable time to burial of children and adults according to religion and the country of residence of participants Group 1 = Muslims in Libya Group 2 = Muslim (in UK) Group 3 = Non-Muslim (in UK)

Religion/ Residence*	**Time to Burial (Child)**					**Time to Burial (Adult)**				
	< 12 hrs	**12-24 hrs**	**1-3 days**	**4 -7days**	**>7days**	**< 12 hrs**	**12-24 hrs**	**1-3 days**	**4 - 7days**	**>7days**
Group1	101	37	0	0	0	62	54	22	0	0
Group 2	21	13	11	0	0	12	17	16	0	0
Group 3	9	18	43	34	33	4	11	43	29	50

*** p values:**

Child Burials	**Adult Burials**	**Child versus Adult Burials**
Group 1 Vs Group 2: $p < 0.001$	Group 1 Vs Group 2: $p < 0.011$	Group 1: chi-squared test was statistically significant at $p < 0.001$
Group 2 Vs Group 3: $p < 0.001$	Group 2 Vs Group 3: $p < 0.001$	Group 2: chi-squared test was statistically significant at $p < 0.001$
Muslims (All) Vs Group 3: $p < 0.001$	Muslims (All) Vs Group 3 $p < 0.001$	Group 3: chi-squared test was statistically significant at $p < 0.001$

Muslims in Libya preferred more rapid burial, particularly for children; 77% of Group 1, 16% of Group 2 and only 7% of Group 3 preferring to bury a child within 12 hours of death ($p < 0.001$).

More of Groups 1 and 2 (88% and 91% respectively) than Group 3 (72%) felt that autopsy leads to an unnecessary delay in burial ($p < 0.001$, Table 2.2, Page 70). More non-Muslims were unconcerned about the impact of traditional autopsy on the dignity of the corpse than Muslims (Table 2.3, Page 61, Figure 2.2, Page 62).

Table 2-3. Respondents' impression of investigations that lead to delay in burial and preserve the dignity of the corpse

Causes an Unacceptable Delay in Burial n (%)				
Post-mortem method	**Muslims in Libya (Group 1)**	**Muslims in UK (Group 2)**	**Non-Muslims in UK (Group 3)**	**p- value**
CT	6 (4%)	0 (0%)	27 (20%)	p<0.001
MRI	11 (8%)	4 (9%)	32 (23%)	P=0.001
Autopsy	122 (88%)	41(91%)	99 (72%)	p<0.001
Dignity of the corpse				
CT	59 (43%)	30 (67%)	70 (51%)	0.019
MRI	85 (62%)	29 (64%)	73 (53%)	0.264
Autopsy	3 (2%)	3 (7%)	22 (16%)	< 0.001

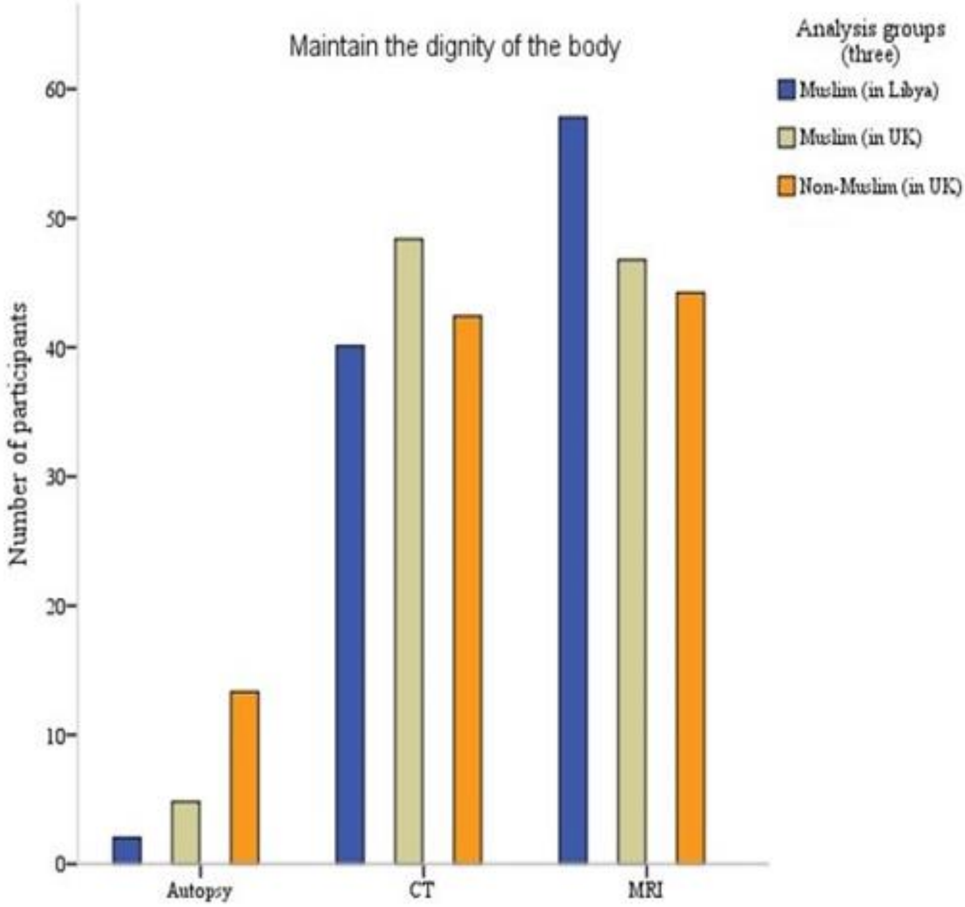


Figure 2-2. Post-mortem methods investigation that preserve the dignity

The ability of post-mortem imaging to preserve the dignity of the corpse was independent of religion, however Muslims felt differently about the emotional impact of autopsy, with 93%, 98% and 64% of Groups 1, 2 and 3 respectively, responding that autopsy has a negative emotional effect on the family ($p < 0.001$, Figure 2.3, Page 63).

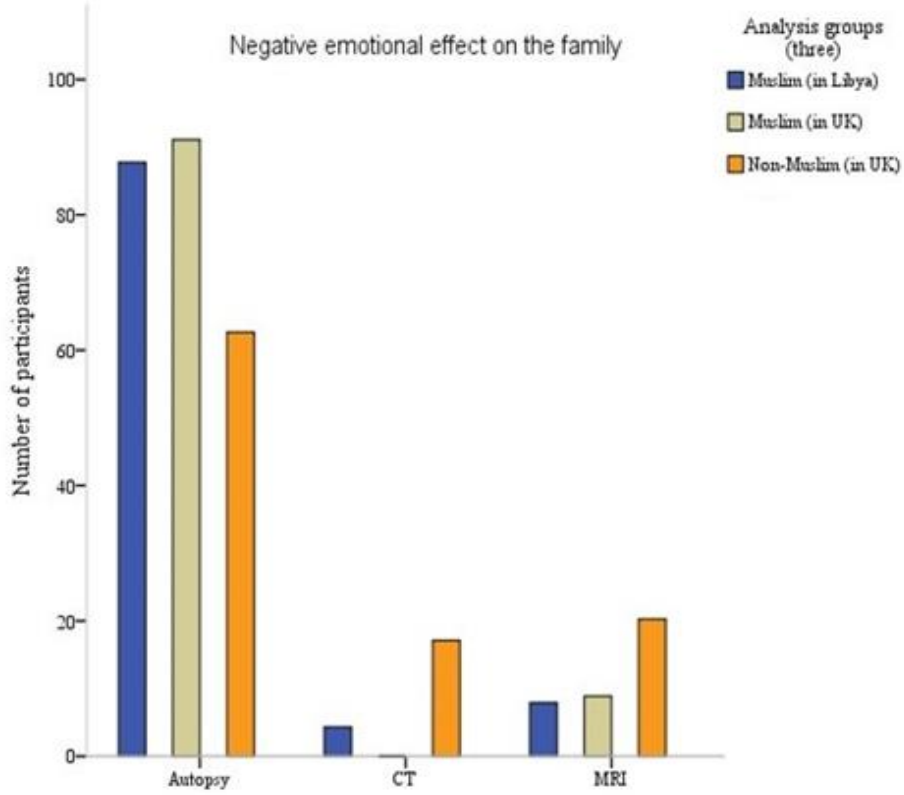


Figure 2-3. Post-mortem methods lead to a negative emotional effect on the family

In terms of identifying the cause of homicidal deaths, 58% of Group 1, 64% of Group 2 and 52% of Group 3 felt that autopsy should be used (p = 0.289). In contrast, 42% of Group 1, 47% of Group 2 and 26% of Group 3 preferred the use of CT to investigate the causes of natural and unexplained death (p = 0.004), while no respondent from Group 1, 2% of Group 2 and 16% of Group 3 preferred conventional autopsy to investigate natural expected deaths (p < 0.001). Finally, 31% of Group 1, 51% of Group 2 and 52% of Group 3 (p = 0.001) preferred the use of MRI over autopsy to investigate the causes of suspicious deaths (Table 2.4, Page 64). There was a significant difference in annual income between Muslim and non- Muslim respondents (p < 0.001), however, there was no difference in salary between those who approved of conventional autopsy and those who did not (p=0.894).

Table 2-4. Respondents' preference for post-mortem investigation depending on nature of death

Modes of death				
		Homicide/Suicide death		
Religion groups	**Group 1**	**Group 2**	**Group 3**	**p value**
CT	21%	33%	48%	< 0.001
MRI	22%	42%	41%	0.001
Autopsy	58%	64%	52%	0.289
Religion		**Natural, but unexplained deaths**		
	Group 1	**Group 2**	**Group 3**	**p value**
CT	42%	47%	26%	0.004
MRI	40%	64%	39%	0.008
Autopsy	20%	9%	53%	< 0.001
Religion		**Natural and expected**		
	Group 1	**Group 2**	**Group 3**	**p value**
CT	65%	73%	15%	< 0.001
MRI	37%	38%	26%	0.119
Autopsy	0%	2%	16%	< 0.001
Religion		**Suspicious deaths**		
	Group 1	**Group 2**	**Group 3**	**p value**
CT	38%	40%	37%	0.903
MRI	31%	51%	52%	0.001
Autopsy	33%	36%	32%	0.935

2.5 Discussion

The recent Arab uprising has been associated with considerable damage to infrastructure and a significant number of people have been killed (Daw et al., 2015); a total of 21,490 persons were killed in Libya between February 2011 and February 2012. Due to the high number of criminal offences and the limited number of consultant pathologists in Libya, there are difficulties with investigating and explaining the circumstances of death(Araby, 2016). Post-mortem imaging may play an important role.

As far as we are aware, this study is the first to formally evaluate the acceptability of PM CT and MRI of Libyan Muslims and UK Muslims of Libyan descent with that of non–Muslim UK residents.

This study shows that both Muslims and non-Muslims perceive conventional autopsy to have a negative emotional effect on family members due to its invasiveness and (for Muslims) the delay to burial that it causes.

Most non-Muslim participants had heard about post-mortem imaging compared to only a small minority of Muslims (mainly doctors and/or those resident in the UK). By comparison, most Muslim and non-Muslim participants were aware of conventional autopsy as an investigational procedure.

These differences in awareness between Muslim and non-Muslim participants may be attributed to the fact that several UK healthcare providers now routinely offer post-mortem MRI in children and PMCT in adults and that some families may have participated in or have been aware of previous/on-going diagnostic accuracy studies of PM imaging. In Libya on the other hand, conventional autopsy is the only available means of PM investigation. We pre-empted this lack of awareness when distributing the questionnaires by providing a short background to conventional autopsy, PMCT and PMMRI as an introduction to the questionnaire.

The time to burial of the body is important in the Libyan culture and is an essential issue for the Muslim family of the deceased, since the culture enforces the religious belief that the body should be buried as soon as possible to reduce the emotional effect on the family and to respect the deceased. It is clearly demonstrated in this study that Muslim participants in Libya support this view, with a significant number feeling that burial should occur within 12 hours of death. This contrasts with the views of non-Muslims, for which no respondent felt that burial was necessary within 24 hours of death and that delays of up to a week were acceptable. Age appears to be negatively related to time of burial but is best interpreted as an artefact of the data collection, where UK Muslims tended to be older than Libyan Muslims and UK non-Muslims i.e. there is a lack of mature non-Muslims in our study population. These views were irrespective of sex. Of interest, more Muslims in the UK had no concerns if burial was delayed for up to 3 days following death. This might be due to differences in the process of obtaining approval for burial and/or due to their living in the UK and assimilating the views of that population. Our results support those of Gatrad et al., that Muslims prefer to bury the body immediately or as soon as possible after death (Gatrad, 1994, Black, 1987). Another study showed that three days is generally considered the maximum delay before burial of a body in the Muslim world (Mohammed and Kharoshah, 2014), which is in keeping with the attitudes of the Muslims we surveyed in the UK. Lishimpi et al. (2001), who studied the guardians and parents of deceased children in Zambia, also found that concerns about time delay before burial had an influence on decisions to refuse an autopsy, although the religion of their study participants was not provided (Lishimpi et al., 2001). Only a small number of Muslim participants in our study thought (perhaps incorrectly) that CT and MRI could lead to unnecessary delay to burial.

“Mutilation” of the body is an important reason that might lead a family to refuse a PM examination (Puranik et al., 2014) along with a fear that organs might be sold for transplantation (Lishimpi et al., 2001). Less invasive methods such as medical imaging can help maintain the body’s dignity, which Muslim and non-Muslim participants of this study also believe. On the other hand, non-Muslim participants were more prepared to accept that a conventional autopsy would not violate the body’s dignity and here, the influence of religion is clearly seen. This result is supported by Ben-Sasi et al. who pointed out that generally, traditional autopsy was perceived comparatively favourably (scored 8 out of 10), with certain demographic factors affecting the overall autopsy acceptability, including ethnicity (more Caucasian and African individuals preferred autopsy compared to Asian or Arabic individuals) and religion (Christians and those with no religious beliefs found autopsy more acceptable than did those of Muslim or Sikh faiths) (Ben-Sasi et al., 2013). Other studies supporting our results include 1) Lynch, who found that Hindus and those of other religions are considered to have a less intrinsic objection to autopsy than Muslims (Lynch, 1999). 2) Cox et al who reported from Uganda, that 59% of relatives (Muslim and non-Muslim) were opposed to autopsy for reasons including delayed burial, body mutilation and associated reasons of a religious nature. Furthermore, the rate of autopsies decreased by approximately 9% due to cultural beliefs and fears that it might lead to infertility among women (Cox et al., 2011). 3) Loughrey who showed that relatives and parents might not consider the benefits of an autopsy and may prefer to “maintain the physical dignity” of their loved one, rather than define the precise cause of death (Loughrey et al., 2000) and 4) Parmar and Rathod, most of whose study participants refused conventional autopsy due to the delay in burial and concern about the cutting of the body or removal of organs (Parmar and Rathod, 2013). Furthermore, consenting to post-mortem examination, especially for infants or children, is psychologically distressing for all guardians involved.

Despite the overall preference for PM imaging over conventional autopsy, it was interesting to find that Muslim participants preferred conventional autopsy for the investigation of homicides and PM imaging for the investigation of unsuspicious deaths. This might imply more belief, by Muslims, in the intrinsic superiority of conventional autopsy to identify the cause of any death. This might not be a misguided belief, since Hussain et al showed that autopsy explained 78% of cases of homicidal deaths (Hussain et al., 2006). On the other hand, PMMRI has been shown to be accurate in detecting abnormal pathology in fetuses (sensitivity 77%, specificity 95%), with slightly lower specificity and sensitivity in children (Arthurs et al., 2014), while PMCT identified the main pathologic process leading to death in 39 of 40 adults (Ross et al., 2012), such that in certain instances, PM imaging is not inferior to conventional autopsy.

This study included 15 physicians (all Muslim) who did not respond significantly differently to the non-physicians. It has been shown that some physicians find the request from relatives for PM examination of a loved one, to be one of the most difficult and unpleasant quarters of paediatric medical practice (Cox et al., 2011). Interestingly, in their survey of general practitioners and clinicians, Midelfart and Aase showed that the number of doctors participating in their study who found that the value of autopsy had decreased due to improvements in CT and MRI techniques was 81%

and 71% for each modality respectively (Midelfart J, 1998). It can be argued that the value of autopsy has not decreased and should not be a case of performing one or the other technique, but rather that PM imaging should be viewed as an adjunct to conventional autopsy or an alternative when consent for conventional autopsy is withheld. (Cohen et al., 2015, Whitby et al., 2015).

Roberts et al. pointed out that the cost implications of PM imaging may be a concern; MRI in particular is more expensive than traditional autopsy (Roberts et al., 2012). In Group 1, the average salary was particularly low and in Libya, healthcare is paid for by the individual. It might be expected that in Libya, caution over the cost of MRI would be a concern, which is congruent with over half of the people in Group 1 being cautious of using this technique. A similar caution may be applied to CT. Healthcare in the UK is free at the point of delivery and therefore cost is not necessarily of personal concern to the individual. Sex had no effect on the results of the survey. As far it is known, there are no published studies that have previously measured the impact of variables such as sex and income on the acceptance rate of autopsies.

This study has several limitations. Firstly, although there were high response rates of 94% from Muslims and 70% from non-Muslims, the precise reasons for those who received but did not return their questionnaires are not available, since attempts were not made to contact these. There may therefore be self-selection bias (particularly amongst non-Muslims). However, response rate does not necessarily determine the validity of a survey (Morton et al., 2012). Even if response rates are low, with careful planning questionnaire surveys may provide high quality data. The anonymous nature may encourage participants to give more frank and credible answers than (for example) interviews, thus helping to reduce bias (Williams, 2003). Probably of more significance than determining reasons why some did not respond, is the fact that we used a non-validated questionnaire. Although the process of validating a questionnaire is time-consuming, it does improve the reliability and accuracy of the collected data (Smit et al., 2012). As part of the validation process, it is also recommended that a pilot study of the questionnaire be conducted. The utility of both validated and non-validated questionnaires is improved when the following conditions are met (as in the current study): the target audience, even if geographically spread apart, can be easy defined and identified; the majority of participants understand what is being asked of them; and the focus of the analysis is numerical i.e. the questionnaire provides quantitative data (Jack and Clarke, 1998). A final limitation of the study is that the questionnaire was distributed to Libyan Muslims in only two countries; Muslims from (or living in) other countries might have responded differently (as indeed might non-Muslims from or living in other countries). Future steps include validating the questionnaire and repeating the study in other populations.

2.6 Conclusion

Religious beliefs and age of the deceased (child versus adult) affect individual preference for PM investigational methods. The preference amongst Muslims for PM imaging is mainly related to the perception that it leads to less delay to burial and is less invasive. Interestingly, conventional autopsy is preferred by Muslims when the cause of death is suspicious. Muslims resident in the UK have an attitude closer to that of the indigenous (non-Muslim) population and therefore in conjunction with developing expertise in performing and reporting on post-mortem imaging investigations, educational programmes may be successful in changing attitudes of Muslims in Libya and other predominantly Muslim countries.

3. Chapter Three

3.1 Comparing the accuracy of post-mortem computed tomography with conventional autopsy in identifying the cause of death in infants and children: A systematic review

3.1.1 Abstract

The aim of this study was to compare the efficacy of post-mortem computed tomography (CT) with conventional autopsy for identifying the cause of death in infants and children. A systematic review was performed by searching the Medline (PubMed) and Embase databases. The publication dates were restricted to between 1970 and February 28th, 2018 and included only papers published in English. Two reviewers independently assessed the eligibility of identified papers. Case reports and original articles that did not include either CT or conventional radiography, studied adults, recruited live patients, studied traffic accidents or used contrast media were excluded.

The review identified 3 eligible papers totalling 262 patients aged from < 1 to 15 years old with confirmed cause of death. Over all the agreement between post-mortem CT and conventional autopsy was 51%. Two reviewers independently assessed the quality of the 3 included papers. Outcomes were described in terms of the percentage agreement for the abnormalities/causes of death detected. Concerning the musculoskeletal system, PMCT identified more abnormalities (44) than autopsy (32). Concerning the brain, PMCT identified more abnormalities (18) than autopsy (10). Concerning the respiratory system, PMCT detected fewer abnormalities (26) than autopsy (37). While PMCT may be a promising method for detecting causes of death/abnormalities related to the musculoskeletal system and brain, over all concordance between PMCT and conventional autopsy was only 51%, with poor agreement (Kappa = -0.18). We conclude that the choice of post-mortem imaging

modality in children may depend on the suspected cause of death; if expertise and costs allow, both PMCT and PMMRI should be considered in all cases.

Abbreviations (CT): computed tomography. (MRI): magnetic resonance imaging. (PM): post-mortem

3.1.2 Introduction

Conventional autopsy with histological and macroscopic investigation is offered to families to help identify the cause of death in children and infants. Except in forensic cases, parental informed consent is required for an autopsy in children following unexpected death (Thayyil et al., 2009b). However, over the last three decades, autopsy rates across the world have declined by 40 to 50 per cent (in children and adults). This decline is attributed to religious, cultural and emotional factors (Stawicki et al., 2008).

Conversely, medical imaging (magnetic resonance imaging (MRI) and computed tomography (CT) is being used increasingly for forensic examinations (Thali et al., 2004). Many studies have explored the use of post-mortem CT and MRI (PMCT, PMMRI) to diagnose the cause of death in adults (Roberts et al., 2012). For instance, post-mortem imaging has been found to be superior to conventional autopsy in the identification of intracranial pathology, pneumothorax and following trauma (Pomara et al., 2009). PMCT may detect more bone lesions than autopsy, particularly in trauma cases. However, CT provides poorer soft tissue contrast and spatial resolution than MRI (Arthurs et al., 2016), although this is off-set to some extent by the ability to separately view soft tissue and bone settings.

In children, PMMRI may have more potential than PMCT. Thayyil et al. (2013) determined that the concordance between minimally invasive autopsy MRI and conventional autopsy to identify the cause of death or a major pathological lesion was 89% in fetuses and children (Thayyil et al., 2013). In comparison, Arthurs et al (2016) found that CT was unable to identify the major causes of death in fetuses of less than 24 weeks gestation, due to poor quality resolution compared to MRI, which provided slightly higher accuracy than CT (Arthurs et al., 2016). Some authors suggest that CT is particularly useful for identifying inflicted injuries, providing superior sensitivity in respect to the identification of rib fractures, which have a high specificity for abuse (Wootton-Gorges et al., 2008, Lederer et al., 2004).

Given the benefits of availability, cost and speed, this review sought to evaluate the extent of agreement between CT and conventional autopsy for identifying the cause of death in infants and children.

Coroner's post-mortem

In England, Wales and Northern Ireland, a 'medico-legal' (involving both legal and medical aspects) post-mortem examination can be instructed by a coroner in certain circumstances. This is called a 'coroner's post-mortem' and is the most commonly performed type of post-mortem. It is carried out under the authority of a local coroner to find out how someone has died. Coroners are usually lawyers or doctors with a minimum of five years' experience.

The police or a doctor may report the death to a coroner if the:

- Cause of death is unknown
- Person who died was not seen by a medical practitioner during their final illness
- Person who died wasn't seen by the doctor who signed the medical certificate within 14 days before death or after they died
- Death was violent or unnatural
- Death was sudden and unexplained
- Death occurred during an operation
- Death occurred before the person came out of an anaesthetic
- Medical certificate isn't available

- The medical certificate suggests the death may have been caused by an industrial disease or industrial poisoning.

They will not be asked for parent's consent for a coroner's post-mortem. However, the coroner must tell them when and where the post-mortem will take place. Also, in some countries all Coroner's work is called "forensic".

Most Coroners in England and Australia are legally trained. Their job is to preside over death investigations and provide pieces of evidence when the death is suspicious, there is a need to identify the deceased, the death is of an unknown cause or the death appears to be violent or unnatural (Barnes, 2003).

3.1.3 Search strategy

The search strategy for this literature review was developed to identify relevant publications in Medline (PubMed) and Embase. The keywords used to conduct the search were (Autopsy) OR (Necropsy) and (Post-mortem) OR (Post-mortem) and (CT) or (CAT scan) OR (Multi-slice computed tomography) OR (Computed Tomography) and (Child) OR (Children) OR (Infant). The publication dates were restricted to between 1970 and February 28th, 2018 and included only papers published in English. Articles that were case reports or reviews, did not include PMCT, studied adults, recruited live patients, recruited children involved in traffic accidents, used contrast media or did not involve an autopsy were excluded. This filtered search identified 358 articles; 322 were excluded; (on the basis of title and/or abstract (306); used MRI (6), not all cases had autopsy (3) or were not in English (1) (Jackowski et al., 2005, Kibayashi et al., 2005, Oyake et al., 2006, Hillewig et al., 2007, Dedouit et al., 2008b, Aghayev et al., 2008, Dedouit et al., 2011, Hong et al., 2011, Hilmes et al., 2011, Michiue et al., 2013, Kano et al., 2015, Sieswerda-Hoogendoorn et al., 2013)A total of 36 full text articles were retrieved, of which 33 did not meet the inclusion criteria (wrong age range (28), not all cases had autopsy (3) did not present clear results (1) or aimed to distinguish live from still birth (1) (Table 3-1, Page 77). (Figure 3-1, Page 78) shows the PRISMA flow diagram for article selection for this review.

Table 3-1. Shows 33 studies did not meet the inclusion criteria.

No	Author	Year	Reason for exclusion
1	Aghayev	2008	Wrong age range
2	Ambrosetti	2013	Wrong age range
3	Andenmatten	2008	Wrong age range
4	Arthurs	2016	Did not present clear results
5	Bedford	2012	Wrong age range
6	Blanc-Louvry	2013	Wrong age range
7	Chen	2008	Wrong age range
8	Como et al	2011	Wrong age range
9	Dedouit	2008	Wrong age range
10	Filograna	2011	Wrong age range
11	Gupta	2010	Wrong age range
12	Hoey	2007	Wrong age range
13	Ieth	2009	Wrong age range
14	Iwase	2010	Wrong age range
15	Lai	2012	Wrong age range
16	Le Blanc-Louvry	2013	Wrong age range
17	Leth	2009	Wrong age range
18	Leth and Christoffersen	2008	Wrong age range
19	Li	2009	Wrong age range
20	Li et al	2009	Wrong age range
21	Marinetti	2005	Wrong age range
22	Marsh	2003	Wrong age range
23	Noda	2013	Not all autopsy
24	Plattner	2003	wrong age range
25	Reiser	2012	Not all autopsy
26	Schulze	2013	Wrong age range
27	Sebire	2006	Wrong age range
28	Shiotani	2002	Wrong age range
29	Sieswerda-Hoogendoorn	2015	Not all autopsy
30	Sowell	2007	Wrong age range
31	Takahashi	2012	Wrong age range
32	Thayyil	2011	Wrong age range
33	Visser	2012	Wrong age range

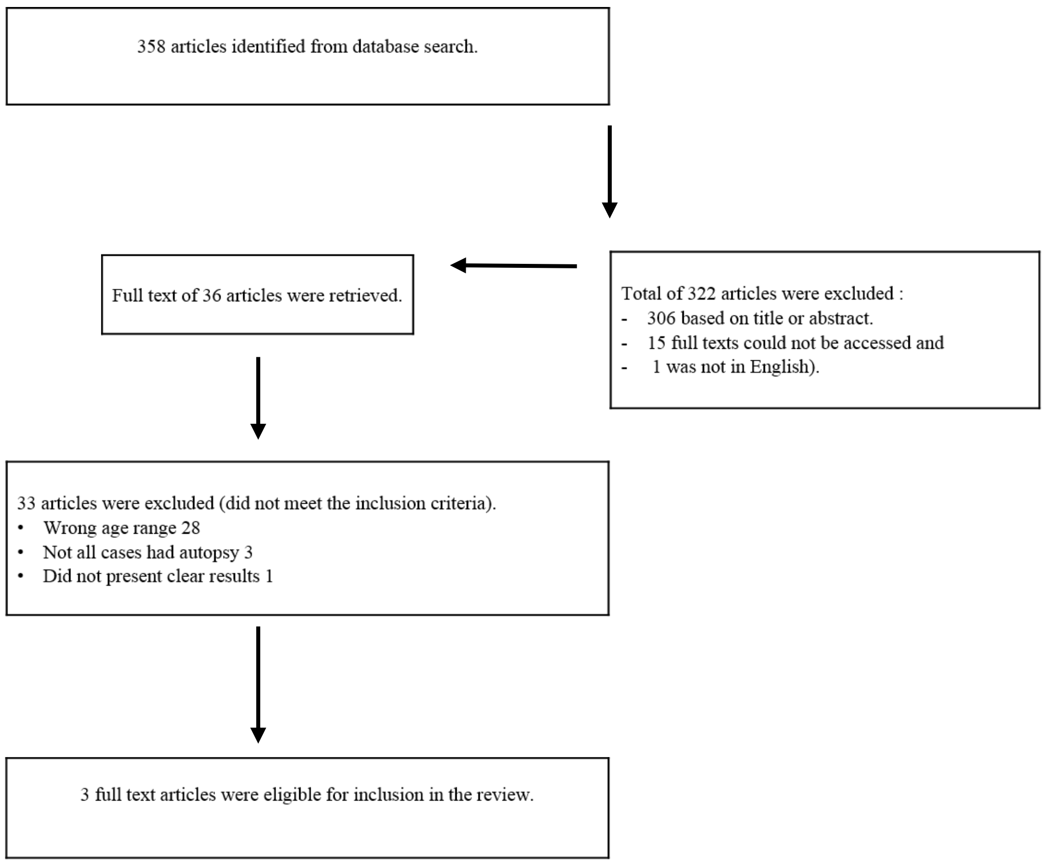


Fig 3-1. Shows PRISMA flow diagram for article selection for this review.

3.1.4 Statistical analysis

There is no formal test to assess the level of agreement and confidence intervals were not reported due to complexity of calculating them when there are 0% agreements. Rather, we have reported chance-corrected agreement as estimated by Kappa for all findings (Rigby, 2000).

Quality Assessment

Two reviewers independently assessed the quality of included studies using the tool developed by the National Institute for Health and Care Excellence (NICE, Appendix G) (Soltanifar and Russell, 2012). Discrepancies were resolved by discussion. The tool considers five aspects of a study; population, method of participant selection, outcomes and analysis of the study. Then, an overall study quality grading is given to each study for internal validity (IV) and a separate grading for external validity (EV).

Results

Data from the 3 studies were extracted by two reviewers. The studies included a total of 262 patients, all of whom had PMCT as their only investigation other than autopsy. Age range was <1 to 15 years (Table 3.2, Page 80).

Table 3-2. The 3 articles included in this review

Reference number	**Year of Publication**	**First author**	**Journal**	**Patient age**	**Number of cases**
1	2016	Beatriz V. Krentz	International Journal of Legal Medicine	< 1–12 years	26
2	2014	T.Sieswerda-Hoogendoorn	Forensic Science International	1-15 years	189
3	2013	Maïa Proisy	European Journal of Radiology	< 2 years	47
	Total				262

The period between the time of death and CT varied from 2 to 72 h. Standard autopsy was performed of the brain, chest, abdomen, and pelvis with all internal organs being examined. Standard CT was performed with a multi-slice computed tomography (MSCT) system, imaging from the skull to the pelvis, the distal femur or the toes, with multiplanar reconstructions. The protocols for CT varied widely between studies regarding the type of CT machine (8- to 64-slice CT systems); slice thickness (between 1.25 and 5 mm for the head and neck); gantry rotation and table speeds; kilovoltage; and the use of and methods for multiplanar reconstruction (Table 3-3, Page 81) summarises the protocols.

Table 3-3. Summary of the CT Protocols used for the Included Studies

CT parameters	PMCT image Report	Autopsy Report	Author name/reference number
• Philips Brilliance, Cleveland, Ohio, USA 16-slice multi- detector CT 120 kV, 300 mAs, collimation 16 × 0.75, pitch 0.688, rotation time 0.5 s slice thickness 2 mm, increment 1 mm.	The reports were written by pediatric radiologists experienced in post-mortem imaging and using a standardized and exhaustive checklist. **PMCT:** Performed within (2 h 01 min (range, 20 min to 5 h 13 min).	The reports were written in consensus by two board-certified pediatric pathologists or by one forensic pathologist according to a standardized protocol (for the sudden infant death syndrome). **Autopsy:** Performed within (24-72 h).	Proisy (2013)
• Philips Brilliance 64, Philips Healthcare, Best, the Netherlands; or Siemens Sensation 64, Siemens, Erlangen, Germany). In all cases, maximum of 3.0-mm-thin slices,	The reports were written by a forensic pediatric radiologist with 10 years of experience in forensic pediatric radiology. **PMCT:** Performed shortly before autopsy	The reports were written by two forensic pediatric pathologists with 8 and 15 years' experience in pediatric forensics and performed according to the local protocol of the Nederlands Forensic Institute. **Autopsy:** Performed within (0–7 days following death, but in 90% of cases autopsies were done within 2 days).	Sieswerda-Hoogendoorn (2014)
• Eight-row multi-detector CT unit CT LightSpeed 8; GE Healthcare, Milwaukee, WI, USA (kV/mA 120/200, tube rotation 2''	PMCT reports were written by a board-certified pediatric radiologist (about 15 years of experience in pediatric radiology) and a board-certified forensic pathologist who specialized in forensic radiology (about 10 years of experience in forensic radiology). **PMCT:** Performed within (2h-3 days)	All the reports were written in consensus by one forensic pathologist in training and one board-certified forensic pathologist. **Autopsy:** Performed within (3h-3 days).	Krentz (2016)

3.2 Summary of Studies

Proisy et al. (2013) compared PMCT to conventional autopsy in identifying the cause of death in 47 cases of sudden unexpected death in children (44 under two years old) between March 2005 and May 2011. PMCT showed a concordance rate of 61.7% as unexplained in 29 cases of death with autopsy.

Sieswerda-Hoogendoorn et al. (2014) (Sieswerda-Hoogendoorn et al., 2014) assessed the accuracy of PMCT in determining the cause of suspicious death in children who also underwent a forensic autopsy in the period January 1st 2008 to 31st December 2012. The total number of cases was 174, but only 98 cases underwent CT. CT and autopsy identified the same cause of death in 69 out of these 98 cases (70% concordance) based on the International Classification of Diseases, (version 2010) (Dugan and Shubrook, 2017). CT showed a high level of agreement with autopsy (59 out of 67 (88%) cases) in unnatural causes of death, but PMCT failed to detect the cause of death in 98% (39/40).

Krentz et al. (2016) reviewed the CT findings from whole body examinations of 26 children (13 male) aged between 0 to 12 years between January 2008 and December 2013. The study was designed to evaluate the performance of CT in identifying the cause of death compared to medicolegal conventional autopsies in children and its prospective usefulness in non-medicolegal situations. All cases underwent CT prior to autopsy, at which 14 cases were diagnosed as natural deaths (7 cases cardiac disease, 1 case multifactorial causes of death, 1 case where the cause of death was related to the digestive system and 2 cases where the causes of death were related to infection). Conventional autopsy was superior to PMCT in identifying cardiac deaths, but PMCT provided more information than conventional autopsy in trauma cases. It detected multiple fractures of the skull, face, a small fracture of the occipital bone and fractures of the right temporomandibular joint, whilst facial, occipital and temporomandibular fractures were missed on autopsy. In addition, PMCT showed a right pneumothorax, which was not identified by autopsy.

Comparison of autopsy and PMCT findings

Table 3.4, Page 84 shows the percentage agreement and which method was superior for detecting abnormalities in the three included studies. PMCT was shown to be superior in identifying bone abnormality such as (2 skull fractures, 1 healing of metacarpal bone, temporomandibular joint 1 and Occipital bone fracture)brain abnormalities, bowel volvulus or perforation, haemothorax and pneumothorax/pleural effusion, whereas autopsy was superior in identifying asphyxia, cardiac disease, infections, lung parenchymal abnormality, liver and kidney malformations, metabolic disease, nerve abnormality and oedema of the mucosa of the vocal cords and Waldeyer's ring. PMCT was able to detect lesions which may not be identified by autopsy. The observed overall agreement was 51% (118 of 138 observations). The number of agreements expected by chance is 138 (50%). This leads to a negative Kappa statistic (chance-corrected agreement) of -0.18, representing poor agreement between CT and autopsy.

Table 3-4. Agreement between PMCT and traditional autopsy

Condition/ System	Identified by Autopsy (N)	Identified by CT (N)	Concordance between CT and Autopsy (%)	Superiority	Agreement (Kappa)	Reference(s)
Asphyxia	2	0	0.00%	+2 Autopsy	Kappa=-1	Krentz (2016)
Fractures	32	43	74%	+11 CT	Kappa=0.25	Krentz (2016), Proisy (2013)
Brain	10	18	56%	+ 8 CT	Kappa=0.44	Krentz (2016), Proisy (2013)
Bowel	2	3	66.7%	+1 CT	Kappa=0.33	Krentz (2016) and Proisy (2013)
Cardiac	19	2	11.00%	+17 Autopsy	Kappa=-0.89	Beatriz V. Krentz (2016) and Proisy (2013)
Infectious	7	0	0.00%	+7 Autopsy	Kappa=-1	Proisy 2013, Tessa Sieswerda-Hoogendoorn (2014) and Krentz (2016)
Lung	37	26	70%	+11 Autopsy	Kappa=-0.29	Proisy (2013) and Krentz (2016)
Liver and kidney malformations	4	0	0.00%	+4 Autopsy	Kappa=-1	Krentz (2016)
Metabolic disease	1	0	0.00%	+1 Autopsy	Kappa=-1	Proisy (2013)
Nerve abnormality	3	0	0.00%	+3 Autopsy	Kappa=-1	Krentz (2016)
Oedema of the mucosa of the vocal cords & Waldeyer's ring	1	0	0.00%	+1 Autopsy	Kappa=-1	Krentz (2016)
Total	118	92	51%		Kappa=-0.18	

Quality of Papers

Quality assessment (Table 3.5, Page 85) showed that the results of these studies are likely to be valid.

Table 3-5. Quality assessment of the included studies.

Author (year) [Reference]	Population	Method	Analyses	IV*	EV**
Proisy (2013)	++	+	++	++	++
Sieswerda-Hoogendoorn (2014)	++	++	+	++	++
Krentz (2016)	++	+	+	++	++

IV*: internal validity, EV**: external validity

3.3 Discussion

The percentage agreement for detecting abnormality for PMCT and autopsy in this review ranged from 11% to 74%, with the highest concordance being for fractures. This review showed that PMCT can identify fractures better than conventional autopsy. This is especially true in body regions that might not routinely be opened by autopsy, for instance, facial fractures, some regions in the skull and temporomandibular joints. Several studies have pointed out that PMCT has the ability to detect fractures, as autopsy does not usually include examination of the entire skeleton (Scholing et al., 2009, Krentz et al., 2016).

Non-skeletal injuries such as brain oedema and subdural hematoma, small pneumothoraces or haemothorax are difficult to detect by autopsy, but more easily detected with PMCT, also when the images interpreted by the expert radiologist in PMCT images. (Kawasumi et al., 2015, Krentz et al., 2016, Proisy et al., 2013). To reduce these missed findings during autopsy, some studies advocate additional tests such as “the flotation test for the heart and lung mass”. However, these methods are time-consuming and not performed on a routine basis and therefore need education and frequent practice (Guddat et al., 2013). PMCT has the ability to detect abnormalities that may be difficult to detect during autopsy. Furthermore, PMCT may provide useful information to the pathologist before starting the autopsy. The difficulty in detecting some injuries using autopsy alone has led authors to suggest that it is not a valid reference standard and should instead be combined with post-mortem imaging techniques (Sieswerda-Hoogendoorn et al., 2014, Krentz et al., 2016, Proisy et al., 2013).

Interpretation of PMCT images is subject to experience and a ‘learning curve’ and it is possible that the differences in percentage agreement may reduce as more experience is gained using PMCT. Clearly diagnostic accuracy of both techniques will depend on the experience of observers. All 3 papers involved at least one experienced paediatric radiologist. In addition, the differences between the 3 studies for observers experience in image interpretation, PMCT protocol, population size which may affect on actual agreement between PMCT and autopsy. Previous studies have also suggested that forensic training for radiologists may improve their skills (Aghayev et al., 2008, Yen et al., 2007). An example of this would be to highlight the need to investigate and identify the location of fractures.

Pneumonia, cardiac disease, liver and kidney malformations, nerve abnormalities and oedema of the mucosa are the abnormalities most commonly missed using CT in the identified studies (Krentz et al., 2016, Kawasumi et al., 2015). It may be possible however to detect these abnormalities using other modern post-mortem imaging techniques for example post-mortem magnetic resonance imaging or post-mortem angiography (Proisy et al., 2013).

This review used the NICE tool, which is a validated, generic tool for the assessment of quality of diagnostic accuracy studies. It depends on the fulfilment of individual items addressing potential sources of bias and variation in diagnostic accuracy studies. Quality assessment showed that the three studies were of good quality. This indicates that the results are likely to be valid.

As several studies have now shown PMCT to be superior to autopsy in identifying only certain abnormalities of brain and musculoskeletal system, rather than replacing autopsy, PMCT may be a useful adjunct to conventional examination. Alternatively, it may be more acceptable to relatives and could provide fundamental findings which might be particularly important when parents refuse an autopsy (Proisy et al., 2013). Given the limitations of PMCT identified by this systematic review and that studies suggest PMMRI is superior to PMCT in children (Thayyil et al., 2013, Arthurs et al., 2016), larger studies comparing PMCT and PMMRI are required.

3.3.1 Limitations

Only three studies were eligible for inclusion with case numbers of 26, 189 and 47. Significant heterogeneity amongst these studies meant that it was not possible to perform meta-analysis of their results.

3.4 Conclusion

This systematic review has shown poor overall agreement between PMCT and autopsy. While PMCT detects more fractures and brain abnormalities than traditional autopsy, it fairs less well for identifying conditions such as asphyxia, cardiac disease and infection. As a result, PMCT should be used as an adjunct rather than an alternative to autopsy. Large prospective studies are needed to further investigate both the complementary and/or replacement role of whole-body (PMCT and PMMRI) in infants and children.

4. Chapter Four

4.1 **Evaluating the agreement between post-mortem computed tomography and conventional autopsy in infants and children**

4.1.1 Abstract

Introduction

Non-enhanced post-mortem computed tomography (PMCT) plays an important role in detecting causes of death, particularly in non-medico legal cases where parents' consent is required to perform a conventional autopsy. Consent for autopsy is often difficult to obtain for deceased children and PMCT may be an acceptable alternative. The aim of this study was

- To evaluate the performance of PMCT compared to conventional autopsy in infants and children.
- To compare the reliability between two pediatric radiologists, one who had experience in interpreting whole-body PMCT images and the second one who had no experience.

Methods

We retrospectively reviewed a post-mortem group of 54 children aged 12 hours–15 years who were investigated by both conventional autopsy and PMCT. We compared the findings independently identified on PMCT by two observers with the findings at autopsy. Kappa was performed to evaluate the agreement between PMCT and autopsy for detecting abnormalities in different regions of the body and to evaluate agreement between the two readers’ reports.

Results

The majority of deaths (26, 46%) were due to sudden infant death syndrome (SIDS). Conventional autopsy detected significantly more abnormalities than PMCT and proved to be superior to PMCT, particularly for identifying organ soft tissue abnormalities. However, PMCT was superior at identifying fractures (Kappa 0.623 p = 0.001). Agreement between autopsy and PMCT (first reader) for brain abnormality was good (Kappa 0.674, p = <0.001), for detecting fractures was good (Kappa 0.623, p= 0.001), and between the two radiologists was good (Kappa 0.725, p= 0.001).

Conclusion

This study revealed that PMCT is superior to autopsy for detecting skeletal abnormalities such as fractures. It is therefore clearly indicated for use in cases involving traffic accidents, blunt trauma or suspected child abuse. However, PMCT has less sensitivity than autopsy for detecting non-skeletal pathology and should be seen as an adjunct to, rather than a replacement for traditional autopsy.

4.1.2 Introduction

Autopsy is used to detect the circumstances of death in infants and children. In most countries, clinical autopsies (with macroscopic and histological investigations) are performed only after permission has been granted by the family. The exception to this is in the case of forensic investigations where the investigation may be necessary to identify inflicted causes of death to protect siblings and other children (Rushton, 1994). Identifying suspected inflicted physical abuse injury is a particularly topical and sensitive issue (Hulson et al., 2014). In the UK the autopsy required to investigate A coroner's post mortem examination, a full hospital post mortem examination, a limited hospital post mortem examination, a minimally invasive autopsy (MIA) and/or a post mortem biopsy (Great Ormond Street Hospital for Children, 2013).

In the last three decades, autopsy rates across the world have declined by 40 to 50 per cent (in children and adults). This decline is due to religious, cultural and emotional factors (Blokker et al., 2016). Despite the undisputable utility of autopsy, fewer families are willing to give consent. The commonest parental reasons for refusing to consent to post-mortem examination are the dread of the child being mutilated and that autopsy might not identify the cause of death (Rose et al., 2006). In addition to difficulties related to obtaining consent and cultural and religious objections, autopsy reports are often delayed (Shojania and Burton, 2008).

In recent years, interest in using less invasive methods as an alternative to conventional autopsy in both children and adults has increased. Post-mortem imaging such as post-mortem computed tomography (PMCT) and post-mortem magnetic resonance imaging (PMMRI) are being increasingly used for investigating the causes of death (Cannie et al., 2012b, Ben-Sasi et al., 2013b). In adult care, PMCT has become the standard, including the use of PMCT angiography, which gives excellent depiction of vascular injury and haemorrhage (Roberts et al., 2012) Moreover, a study performed in 2017 pointed out that PMCTA provides more accurate findings than autopsy in PM adult cases (Rutty et al., 2017). Several studies have investigated the use of PMCT or PMMRI to explain the circumstances of death in adults (Roberts et al., 2012, Wichmann et al., 2012) However, PMCT showed less concordance with autopsy in fetuses and children (Arthurs et al., 2016) and is therefore mainly used in adults while PMMRI may be more useful in children (Alderliesten et al., 2003, Nicholl et al., 2007). Imaging autopsy is an acceptable alternative to conventional autopsy (Ben Taher et al., 2018, Klein et al., 2015). For instance, Le Blanc-Louvry et al. indicated that the agreements between PMCT and autopsy is almost perfect in identifying the cause of death, and PMCT might be considered as effective as a forensic standard autopsy in identifying the cause of death in certain traumatic events (Le Blanc-Louvry et al., 2013); Roberts et al. pointed out that PMCT was an even more accurate imaging technique than PMMRI for identifying the cause of death when both were compared to conventional autopsy (Roberts et al.). PMMRI shows excellent agreement with conventional autopsy for identifying abnormality and causes of death in fetal and neonatal cases (Thayyil et al., 2013). The study carried out by Arthurs in 2015 pointed out that PMMRI could be the first option to identify the causes of death in fetuses. PMMRI might provide an alternative to conventional autopsy and has further benefits, such as potentially saving both time and money compared to conventional investigations in adults (Ahmad et al., 2017). There are a number of advantages in using PMCT compared to PMMRI: the major discrepancy rate compared with conventional autopsy was significantly higher for PMMRI than for PMCT; PMCT provides better resolution than PMMRI and is sensitive for detecting brain haemorrhage and fractures; PMCT has important practical advantages as it is less expensive, more widely available, and faster than PMMRI (Arthurs et al., 2015).

However, there have only been a few reports on infants and children of PMCT findings (Proisy et al., 2013, Thayyil et al., 2013, Sieswerda-Hoogendoorn et al., 2014b Kawasumi et al., 2015, Arthurs et al., 2016, Krentz et al., 2016). Therefore, aims of this study

- To evaluate the agreement between PMCT and autopsy to detect abnormalities in different regions of the body or inflicted injuries, which autopsy may not identify infants and children.
- To compare the reliability between two pediatric radiologists, one who had experience in interpreting whole-body PMCT images and the second one who had no experience.

4.1.3 Materials and methods

4.1.3.1 Study group

We selected all consecutive PMCT scans performed in the Department of Radiology at Sheffield Children's Hospital in the period between 20th February 2012 and 24th November 2014 (28 cases) and between 14th October 2016 and 5th December 2017 (28 cases) giving a total of 56 children. All also had post-mortem examinations performed in the Department of Pathology. No child had a known pre-existing disease.

4.1.3.2 Image acquisition

All bodies were stored in a mortuary at 4 °C prior to PM imaging. Whole-body PMCT imaging was performed on a 64-slice multidetector system (A Light speed VCT 64-slice helical CT scanner) by trained radiographers (who perform all PMCT scans at Sheffield Children’s Hospital). Brain PMCT imaging consisted of contiguous 1 mm axial slices with a 5 mm gap at 120 kV and variable mAs. Volumetric whole-body PMCT imaging was then performed from the vertex down to the toes at 120 kV with variable mAs, a pitch of 1, and 0.625 mm collimation. Images were reconstructed with a soft tissue and bone algorithm to provide 5 mm and 1.25 mm slices, and viewed on standard soft tissue, lung, and bone window settings. Further 3D reconstruction of the body was performed on the PACS system at Sheffield Children's Hospital.

4.1.3.3 Image interpretation

Image interpretation for brain, chest, abdomen, pelvis and skeleton was performed. Two paediatric radiologists independently interpreted the whole-body PMCT and skeletal radiographs at Sheffield Children's Hospital. The first reader had 9 years' experience of interpreting PMCT and the second reader had no experience of interpreting PMCT. The cause of death, clinical history and autopsy findings were unknown at the time of image interpretation. Both radiologists were accredited by the Royal College of Radiologists (London, UK). At the time of the autopsy, the pathologist was informed of the subject's clinical history but was blinded to the findings of the PMCT.

Images were interpreted on the PACS system in Sheffield Children's Hospital with two-dimensional transverse, coronal, sagittal and oblique data sets, and three-dimensional volume-rendered images. Supposed cause of death was determined from any abnormal findings seen on the whole-body PMCT images. A diagnosis of unexplained death was given when no cause of death manifested on imaging. In this study observers used an electronic survey platform to write their reports. Although the second radiologist interpreted images in only 43 cases. The radiologists were also blinded to the autopsy results.

All autopsies were systematically done within 20 mints–35 hours after PMCT by a consultant paediatric pathologist or a forensic pathologist following a standardised protocol which included biological investigations and macroscopic and histological examination.

4.1.3.4 Ethical approval

The study was approved by the Local Research Ethics Committee and Health Research Authority (Reference Number SCH/15/064). The need for informed consent from the relatives of the deceased was waived.

Statistical analysis

Kappa statistics were used to evaluate agreement between PMCT and autopsy in determining the cause of death and identifying abnormality. Kappa was also used to evaluate agreement between the radiologists. Statistical analysis was performed using IBM PSS, version 24 for PC.

4.1.4 Results

During the study period, 56 post-mortem infants and children were presented. Of these, two were excluded (in which autopsy was not performed). In total 54 infants and children underwent both PMCT and autopsy. Aged ranged from 12 hours to 15 years (mean 2 years, SD 4.4 years) and 31 (58%) were male.

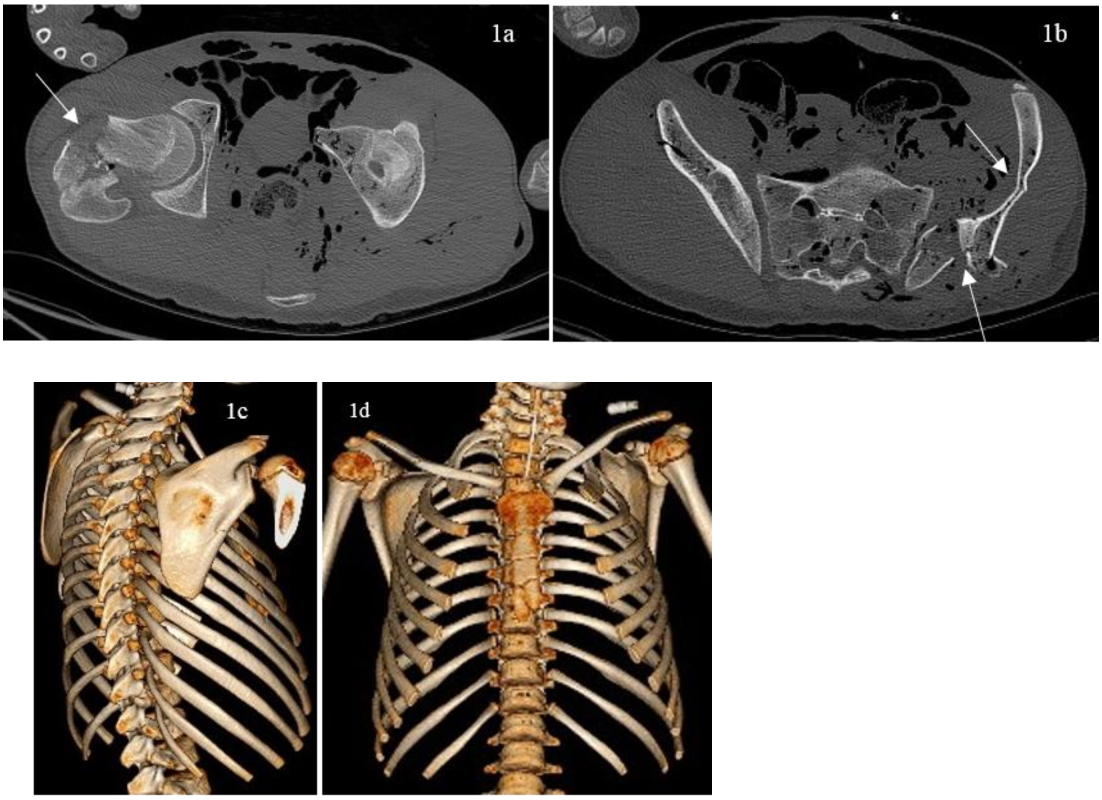


Fig 4-1. Shows (a) Axial PMCT of femoral neck and multiple pelvic fractures in an 15 years old, (4.1b, c and 4.1d) belongs to an 8 years-old male. (4.1b) Right femoral neck, (4.1c) fracture of the body right scapula (4.1d) Right clavicle-middle third

4.1.5 Results regarding the cause of death

Kappa scores are summarised in (Table 4.1, Page 98). There was good agreement between autopsy and PMCT (first reader and second reader) for detecting fractures (0.623, p= 0.001). In addition, the agreement between the radiologists for reporting fractures was very good agreement (Kappa 0.725, p= 0.001). PMCT detected 44 fractures in different regions of the body and provided more information than autopsy. In Case 15, a 12 year-old male who died following major trauma multiple fractures of the pelvis, the right scapula and clavicle were recognised on PMCT but not on autopsy (see Figure 4.1, Page 97). Overall, PMCT showed 21 more fractures than autopsy (see Table 4. 2, Page 99).

Table 4-1. Shows the percentage agreement between autopsy and PMCT to detect abnormality in different organs

Organ	Autopsy = Normal	First reader = Normal	Autopsy = Abnormal	First reader = Abnormal	Total	Kappa
Skeletal	47	45	5	7	52	0.644
Brain	38	43	16	11	54	0.674
Chest	44	44	9	7	53	0.455
Abdomen & pelvises	51	50	2	1	53	-0.028
Organ	**Autopsy = Normal**	**Second reader = Normal**	**Autopsy = Abnormal**	**Second reader = Abnormal**	**Total**	**Kappa**
Skeletal	47	39	5	4	52	0.60
Brain	38	4	16	36	54	0.00
Chest	44	14	9	24	53	0.059
Abdomen & pelvises	51	37	2	3	53	-0.066
Organ	**First reader = Normal**	**Second reader = Normal**	**First reader = Abnormal**	**Second reader = Abnormal**	**Total**	**Kappa**
Skeletal	45	39	7	4	52	0.730
Brain	43	4	11	36	54	0.046
Chest	44	14	7	24	53	0.199
Abdomen & pelvises	50	37	1	3	53	0.481

This study also showed that autopsy detected chest abnormalities in 34 cases compared to PMCT which detected abnormalities in 17 cases - Kappa was moderate (0.455) and the agreement between first and second readers was poor (Kappa = 0.199).

The most common cause of death in this study (46%) was sudden infant death syndrome (SIDS), which was PMCT reported most of them as unknown which can be considered the equivalent of SIDS, 6 cases were hypoxic ischaemic, 3 cases were major trauma and 21 cases had variable causes of death (see Table 4-3, Page 100).

Table 4-2. Fractures identified by PMCT.

Site of fracture	**Number detected by PMCT**	**Number detected by autopsy**
Clavicle	1	0
Digit	3	0
Femur	2	0
Humerus	2	0
Pelvic	8	0
Radius/ulna	2	0
Ribs	19	16
Skull	6	7
Tibial	1	0
Total	**44**	**23**

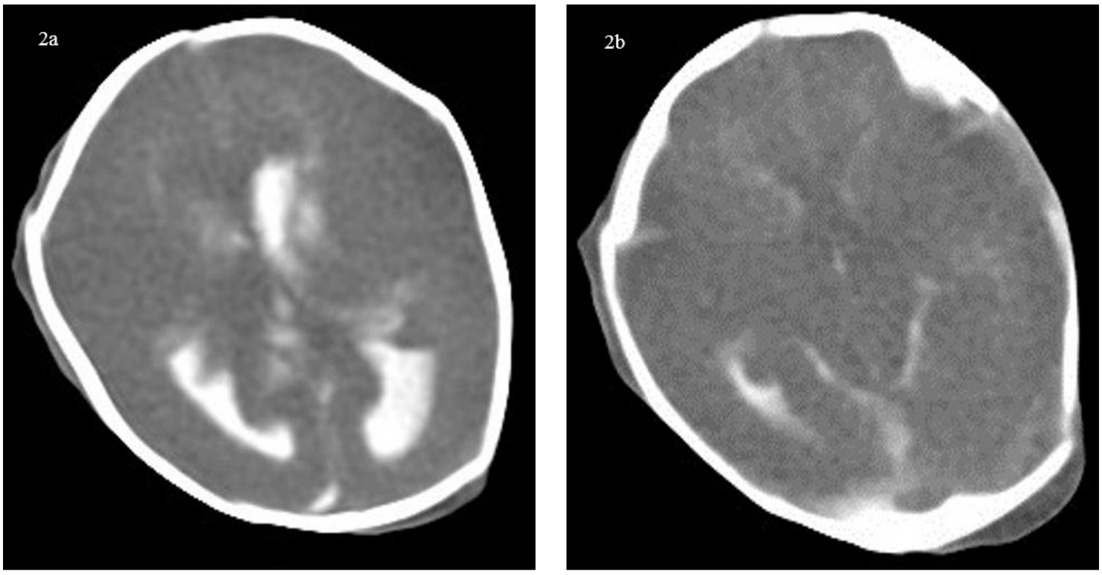
Table 4-3. Cause of death according to autopsy report (Listed in sequential order of presentation

No.	Sex	Age	Cause of death/Autopsy findings	Cause of death/PMCT findings
1	Male	3 weeks	Sudden infant death syndrome	Unknown
2	Female	1 year 9 months	Subdural haemorrhage, retinal haemorrhages and early hypoxic encephalopathy	Unknown
3	Male	1 day	Massive malignant congenital tumour involving the right cerebral hemisphere, hydrocephalus	Massive intracranial bleeding
4	Male	2 years	Methadone toxicity	Unknown
5	Female	7 weeks	Non-accidental injury	Unknown
6	Female	23 days	Sudden infant death syndrome	Unknown
7	Female	4 weeks	Hypovolaemic shock, Superior sagittal sinus haemorrhage, Aplasia cutis congenita	Unknown
8	Male	10 weeks	Sudden infant death syndrome	Unknown
9	Male	19 day	Sudden infant death syndrome	Unknown
10	Female	3 months	Sudden infant death syndrome	Unknown
11	Female	11 days	Sudden infant death syndrome	Unknown
12	Male	7 weeks	Pneumonia	Unknown
13	Male	3 months & 15 days	Sudden infant death syndrome	Unknown
14	Male	10 weeks	Severe acute bronchopneumonia	Unknown
15	Male	5 months	Sudden infant death syndrome	Unknown
16	Male	3 months & 15 days	Cardiomyopathy	Unknown
17	Male	3 months	Sudden infant death syndrome	Unknown
18	Female	15 days	Hypoplastic left heart syndrome	Unknown
19	Male	1 year	Sudden infant death syndrome	Unknown
20	Male	1 month	Sudden infant death syndrome	Unknown
21	Female	32/40	Intraventricular haemorrhage, acute chorioamnionitis	Unknown

22	Female	23 months	Delayed sudden unexpected death in childhood	Unknown
23	Female	12 Hours	Hypoxic-ischaemic encephalopathy and multi-organ failure. (b). Maternal and transplacental paracetamol	Unknown
24	Male	2 years & 11 months	Fresh water drowning and hypothermia	Unknown
25	Female	4 weeks	Bilateral diffuse acute intra-alveolar haemorrhage. Staphylococcus aureus bacteraemia/sepsis	Unknown
26	Female	37 weeks	Stillbirth	Unknown
27	Male	2 years & 7 months	Sudden infant death syndrome	Unknown
28	Male	5 years	Choking on food	Unknown
29	Female	14 years	Cardiac hypertrophy	Unknown
30	Male	4 months	Hypoxic ischemic encephalopathy. Bronchopneumonia.	Unknown
31	Male	1 month	Sudden infant death syndrome	Unknown
32	Female	12 years	Acute liver failure	Unknown
33	Male	8 weeks	Sudden infant death syndrome	Unknown
34		12 weeks	Sudden infant death syndrome	Unknown
35	Female	6 weeks	Sudden infant death syndrome	Unknown
36	Female	14 months	Sudden infant death syndrome	Unknown
37	Male	1 year & 6 months	Sudden infant death syndrome	Unknown
38	Male	11 weeks	Sudden infant death syndrome	Unknown
39	Female	15 years	Brain tumour	Unknown
40	Male	17 days	Complications of prematurity.	Unknown
41	Female	6 weeks	Sudden infant death syndrome	Unknown
42	Male	15 days	Extreme prematurity	Unknown
43	Male	5 months	Group A streptococcal infection	Unknown
44	Female	5 weeks	Sudden infant death syndrome	Unknown
45	Female	9 weeks	Sudden infant death syndrome	Unknown

46	Male	8 years	Head injury	Brain injury falling major trauma
47	Female	5 weeks	Sudden infant death syndrome	Unknown
48	Male	15 months	Sudden infant death syndrome	Unknown
49	Male	15 years	Multiple injuries	Major trauma
50	Male	12 years	Multiple injuries	Major trauma
51	Male	14 years	Multiple injuries	Major trauma
52	Female	15 years	Brain haemorrhage. Ruptured malformation in the territory of the left middle cerebral artery	Ruptured aneurysm arteriovenous malformation
53	Male	2 years & 8 months	Compression to the neck	Unknown
54	Male	15 years	Sudden infant death in epilepsy	Unknown

This study showed significant agreement between PMCT and autopsy in detecting brain abnormality (0.674, p=<0.001). Both methods detected subdural and intraventricular haemorrhage (Figure 4.2, Page 103).



(2a) Intraventricular haemorrhage a 23 day-old male   2b Subdural haemorrhage a 23 day-old male

Fig 4-2. Shows (a) Axial PMCT shows intraventricular haemorrhage and (b) subdural haemorrhage, in a 23 day-old male

PMCT detected 4 pneumothoraces, 3 on the right (Figure 4.3, Page 104), whereas autopsy detected 1 on the right side and 2 on the left.

Figure 4-3. Axial PMCT in an 8 year-old female showing right and left pneumothorax

4.1.6 Discussion

This study aimed to evaluate the agreement between PMCT and autopsy to detect abnormalities in different regions of the body or inflicted injuries, which autopsy may not identify.

This study showed that, in general, PMCT is superior to autopsy for detecting fractures. Specifically, PMCT can detect fractures at sites which may be difficult to detect by autopsy such as proximal phalanx left thumb, and pelvic fractures such as ischial and pubic fractures. This result is supported by a study in 2013 which found that autopsy may not identify bone abnormalities in areas which are not routinely investigated by autopsy, such as pelvic and facial bones (Christine et al., 2013). PMCT could also be useful in determining the cause of death in children (Christe et al., 2010). From the forensic literature on children, several abnormalities which are important for detecting the cause of death using PMCT have been identified; in 67% of cases, CT provided the same causes of death as those identified by autopsy (Sieswerda-Hoogendoorn et al., 2014).

Previous studies stated that PMCT has been used to detect suspected inflicted injury, especially when rib fractures or brain injury are involved (Dedouit et al., 2008a). In cases of death related to trauma, PMCT may for show, for instance, multiple fractures of the skull, ribs, pelvis and lower limbs (cases 48, and 49). However, this study showed that PMCT has less sensitivity than autopsy to detect overall abnormalities in different body systems or organs.

Autopsy detected subdural haemorrhage in both sides of the brain which was related to inflicted injury, however, one of the readers did not report these findings. Also, the second reader reported some abnormalities which might be related to post-mortem changes. This may be due to the lack of experience of the radiologist in the interpretation of PMCT images. With the development of PMCT imaging, radiologists should gain more expertise with non-specific post-mortem changes in order to differentiate them from specific signs which could explain the circumstances of death (Christe et al., 2010). Interpretation of PMCT images is subject to experience and a ‘learning curve’ and it is possible that the differences in percentage agreement may reduce as more experience is gained using PMCT. Previous studies have also suggested that forensic training for radiologists may improve their skills (Aghayev et al., 2008, Yen et al., 2007).

This study showed the weaknesses of PMCT compared to conventional autopsy. For example, PMCT has limited performance for detecting abnormalities in the parenchyma of organs. Thayyil et al. (2010) stated that unenhanced CT alone could not identify parenchymal and soft tissue findings and to detect soft tissue pathology the injection of a contrast agent (angiography) is required. The disadvantages of PMCT might be overcome by post-mortem intravenous injection of a contrast agent or alternatively by using PMMR; both of these post-mortem imaging techniques have been reported to improve the detection of abnormalities of parenchymal or soft tissue lesions in adult forensic imaging literature (Scholing et al., 2009). Moreover, Grabherr et al. (2018) stated that combining both PMCT and autopsy might increase the quality of detection of abnormalities in post-mortem cases involving the soft tissues (Grabherr et al., 2018). To date, in childhood there is no standardised technique for using PMCT angiography; using these developments might change the diagnostic value of PMCT in childhood, as has been the case in adult forensic post-mortem imaging.

Although detection of abnormalities of the parenchyma and soft tissues using PMCT is less effective than the detection of bone abnormalities, it may also be improved by combining PMCT and autopsy. Interpretation of images of the lung may be difficult due to change related to the length of time the PMCT was performed after death and the post-mortem interval. Historically, a conventional autopsy has been used as the gold standard for detecting pneumonia. However, pneumonia can be seen as a patchy presentation, and the histological lung tissue sample from each lobe of the lung may involve healthy parenchyma of the lung tissue only. In this case, CT guidance could be useful to improve the quality of the autopsy sample taken (Aghayev et al., 2007). Also, some PMCT findings, such as fluid-filled bowel dilatation and diffuse gaseous dilatation (such as in Case 17) may or may not be related to the cause of death. As suggested by recent literature, these results support the idea that the results of an autopsy alone should not be taken as the gold standard for detecting the causes of death; the combination of autopsy and PMCT could be more valuable (Zerlauth et al., 2013, Christine et al., 2013).

In this study, autopsy reported the causes of death in cases of hypoxic ischemic encephalopathy (Case 30), SIDS (46% of cases), cardiomyopathy (Case 18) and cardiac hypertrophy (Case 29), which might be impossible to detect using PMCT. Noda et al. (2013) identified that PMCT imaging of the lungs and airways alone did not provide sufficient data for detecting aspirated material or differentiate between post-mortem or pre-mortem lesions. Moreover, PMCT is not able to differentiate abnormality that may be related to the cause of death e.g. aspiration pneumonia, infections and cardiac failure, from post-mortem changes and/or non-specific findings including pulmonary oedema, pulmonary atelectasis and congestion. There could be a contradiction between conventional autopsy findings and PMCT findings if the cause of death is related to pneumonia (Noda et al., 2013).

Successful PMCT scanning has a number of requirements; the most important of which is the use of a suitable CT scanner. Although whole-body PMCT scan does not take very long, trained personnel are required to both perform (ideally a trained forensic radiographer) and interpret the images. Post-mortem changes in the body will influence the PMCT image interpretation and this information needs to be communicated to the pathologist who is reading the PM results. Based on our study results, we define indications for using PMCT alone to identify the cause of death to be trauma cases (accidental or suspected inflicted injury).

4.1.6.1 Limitations of this study

Our study used data from a small number of cases over a 14 month period. A large-scale prospective study needs to be performed to truly establish the accuracy of PMCT compared with conventional autopsy for identifying the causes of death. Also, the experience of readers of PMCT images is very important for providing useful reports. In this study, the second reader had no experience in interpreting PMCT images which could affect the study results. To improve PMCT reports, the radiologist should have all the background information and results of the external examination, as well as toxicology if requested and performed.

4.1.7 Conclusion

This study revealed that PMCT has less sensitivity to detect some abnormalities than autopsy. However, the results of this study showed that PMCT is superior when compared to autopsy for detecting bone abnormalities such as fractures. It also clearly identified cases involving traffic accidents, blunt trauma and injury related to inflicted physical abuse. PMCT does not however appear to be useful in cases which need findings from macroscopic examination and has limited utility in cases that involve death related to the lung, heart and liver. Identifying causes of death using PMCT alone is thus problematic. Our results suggest that in trauma cases, autopsy alone can no longer be regarded as the diagnostic gold standard and that it should be combined with PMCT.

5. Chapter Five

5.1 Non-Invasive Estimation of Post-Mortem Interval using Computed Tomography

5.1.1 Abstract

Background

Accurate estimation of the post-mortem interval (PMI) may be a matter of crucial importance in forensic investigations.

Purpose

To investigate whether longitudinal changes in organ Hounsfield units (HU) and total body air volume (TBAV), as measured from serial PMCT scans, can provide an estimate of PMI.

Methods

Eight euthanised lambs each had five whole body CT scans performed over seven days and measurements were taken from the brain, heart, lungs, liver, kidneys, spleen, soft tissues around the hips and shoulders, and from both hip and shoulder joints. HU tissue density was measured directly from the PMCT images, while TBAV was calculated using ImageJ software. A random effect model was fitted with the subject fitted as a random intercept. Ethical and Animal Welfare approval was obtained.

Results

- TBAV increased by (1696 mL + 395 mL / day) for each additional day after death, also TBAV / weight (51.325 mL/Kg/day + 231 mL/Kg).
- For each additional post-mortem day, the HU of the brain, heart, lung, liver, spleen and hip and shoulder joints decreased, while HU for the kidneys and soft tissues around the hip and shoulder joints increased

Conclusion

There was clear and progressive decrease in tissue densities and increase in TBAV in individual cases over time. However, this indicates that more work is required before either HU or TBAV can be used as non-invasive methods to reliably determine time of death in humans.

Abbreviations: PMCT, post-mortem magnetic resonance imaging (PMMRI), Hounsfield units (HU), post-mortem interval (PMI), total body air volume (TBAV).

Highlights:

- Measuring organ Hounsfield units has potential to be used as a non-invasive method of estimating post-mortem interval.
- Total body air volume showed significant correlation with post-mortem interval.
- More research is required before CT can be used to determine PMI in humans.

5.1.2 Introduction

The time elapsed since death is important in forensic investigations and the term post-mortem interval (PMI) refers to the interval between the time of death and examination of the body (Cardoso et al., 2010). Different physical (Nelson, 2000), chemical (Bocaz-Beneventi et al., 2002) and biological (Arnaldos et al., 2004) methods are used to estimate duration of death in the early post-mortem period (Gill-King, 1997). The forensic process usually provides PMI primarily based on macroscopic and histologic changes. Decomposition is a natural process that occurs in the tissues of the body and leads to its decay. Degradation of the tissues occurs by microorganism activity, including fungi, bacteria and protozoa, which originate from normal biota in the human body, particularly in the gastrointestinal system. This process continues beyond the dry remains stage, as the bones continue to undergo putrefaction, though at a much slower rate (Hau et al., 2014, Shapiro-Mendoza et al., 2014). The putrefaction products formed by decomposition are in the form of gas, fluid or salt. The types of gas produced include carbon dioxide, sulphide, methane, ammonia, hydrogen and sulphur dioxide (Gennard, 2012).

Post-mortem magnetic resonance imaging (PMMRI) and computed tomography (PMCT) have been widely used in the forensic field, and have several advantages; they are non-invasive (Yen et al., 2007) , the images are easily stored, and available for review if required. They also provide additional support to the autopsy by providing advanced information on the expected findings (Jackowski, 2013).

Hounsfield units (HU) can be measured from CT scans, and represent the attenuation of the x-ray beam by tissues. HU values depend on the composition of the tissue and thickness of the anatomical structures that the beam passes through (Lamba et al., 2014). HU measurement is quick and simple and allows some characterisation of tissue such as cystic lesions, the nature of intraperitoneal fluid and hepatic steatosis for example (Levi et al., 1982). In CT scan images, blood fluids are characterised and differentiated based on HU ranges and magnitudes (Allen et al., 2012). The HU scale is standardised such that the HU value for water is 0 and for air is -1000 at all tube energies used. The radiodensity of blood is ranged between 40 and 60 HU, but the exact HU value depends mainly on the cellular content. The HU of serous fluids range between 15 and 30 HU but the exact HU value depends on the protein content in the cell (Huda and Slone, 2003). PMCT however is vastly different from clinical CT due to the various post-mortem phenomena such as biochemical degradation, diffusion processes and putrefaction (Thali et al., 2003, Dirnhofer et al., 2006).

Determining total body air volume (TBAV) after death using CT scans is feasible using existing software. The relationship between the body's decomposition and the total volume of air might provide a useful non-invasive method to estimate the time of death. PMCT can be used to evaluate gas embolism and to provide indications for gas composition analysis (Egger et al., 2012).

The aim of this study was to determine the utility of measuring 1) organ Hounsfield units (HU) and 2) the volume of gas resulting from the process of decomposition as measures of PMI.

5.1.3 Study design

5.1.3.1 Methods

This was a prospective observational study of eight lambs, one month old at the time of death. Lambs were slaughtered by intravenous pentobarbitone overdose. Time of death was recorded for each animal before being brought to CT at Sheffield Children's Hospital, within approximately three hours after death, to start the scanning protocol.

The lambs were acquired in three groups; with two lambs in the first group and three lambs in each of the second and third groups in order to facilitate the PMCT scanning process and to reduce congestion in the Radiology Department. Each cadaver was double bagged immediately after euthanasia and kept in a covered plastic box (to avoid exposure to flies and rodents) at room temperature of approximately 19°C.

5.1.3.2 Hounsfield unit measurements

Whole body PMCT scans were performed on each lamb on five occasions during the week following death. The lambs were transported daily to Sheffield Children's Hospital for CT scanning and then returned to room storage. A single researcher reconstructed and reformatted the PMCT images. For each lamb, the average HU was recorded by a single observer at six sites from each of the following organs; brain, heart, lungs, liver, spleen, kidneys, soft tissues around the hips and shoulders, and from both hip and shoulder joints. HU was measured from six sites of each organ using the PACS system at Sheffield Children's Hospital and the average of these measurements was calculated (Figure 5.1, Page 117).

ImageJ software (Abràmoff et al., 2004) was used to measure the total body air volume (TBAV) of each lamb at approximately 3, 16, 50, 75 and 160 hours after death. ImageJ software is a machine vision application capable of measuring size and volume. The method of measuring the volume of gas is outlined below:

All images that did not include a body area were excluded from the anaylsis (Figure 5.2a, Page 118). Artifacts were removed by cropping images in each slice in rectangular shape (Figure 5.2b, Page 118). Images were then converted to 8 bit format and contrast was adjusted to maximally distinguish air from soft tissue (Figure 5.2c, Page 118). The software only allows segmentation in to a maximum of two compartments. Therefore a two-step measurement process was adopted. Firstly, for slice 1, body tissue and total air (internal to the body and external to the body i.e environmental) were assigned different colours red and white respectively (Figure 5.2 d, Page 118). The total volume of air in slice 1 (A_1) was measured. In the second step, the external air volume in slice 1 (B_1) was segmented from the image and measured (Figure 5.2d, Page 118; external air = red). Internal body air volume for slice 1 was therefore A_1 minus B_1 = $V_{1.}$ TBAV was calculated as the sum of body air for all slices in the scan.

5.1.3.3 Image acquisition

All CT examinations were performed at Sheffield Children's Hospital, by a trained radiographer, using a Lightspeed VCT 64-slice helical CT scanner and standard scanning parameters of 100Kv and 60 mA. Contiguous axial slices of 0.625mm were obtained and images reconstructed on soft tissue and bone algorithms to provide 5 mm and 1.25 mm thick slices. The total time taken for PMCT image acquisition was less than 5 minutes per study. The scans were reformatted, and the average HU calculated from six sites in each organ at each time point. The picture archiving and communication system (PACS) at Sheffield Children's Hospital was used to measure all Hounsfield units.

5.1.3.4 Ethical approval

Approval was obtained from the Animal Welfare and Ethical Review Body, Nottingham and from of the University of Sheffield Ethics Committee.

5.1.3.5 Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 24 for PC (IBM Corp, Armonk, NY). Multilevel Random intercept models was used to analyse the data for the measurements of Hounsfield units and TBAV. Statistical significance was set at 0.05.

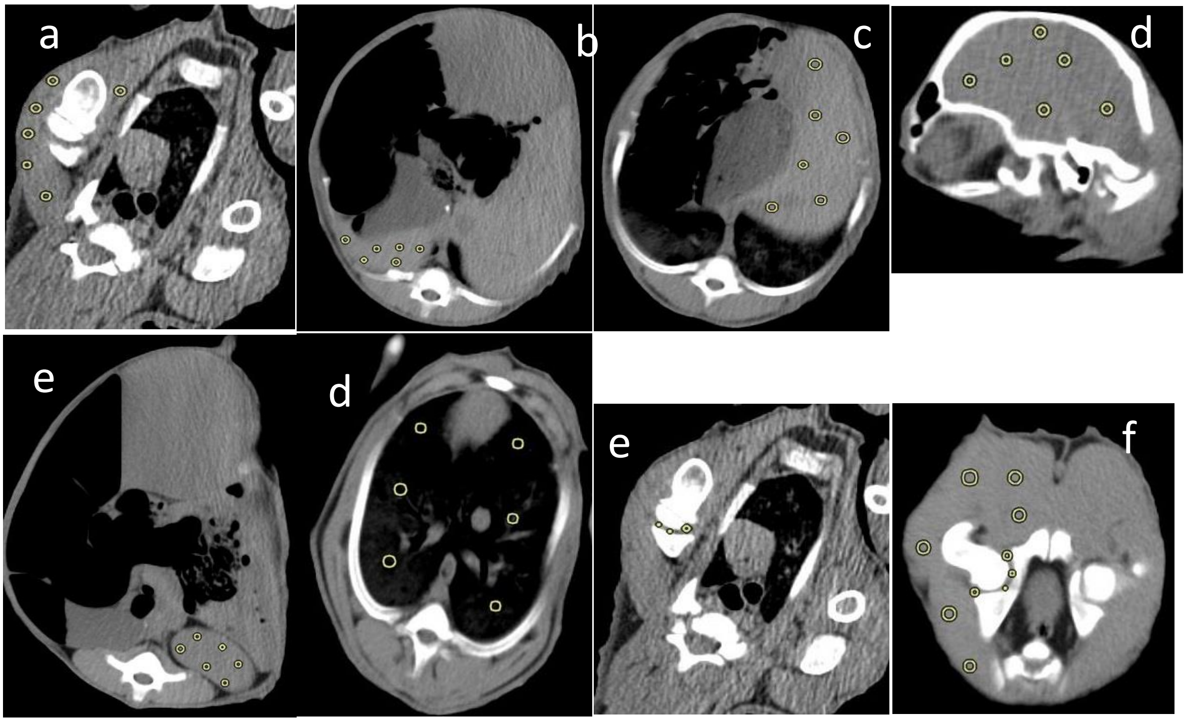


Figure 5-1. Shows the evaluation of radiopacity changes of different organs tissue six regions of interest (ROI) used PACS within each organ as shown in this image. ROI 1: area ≤ 0.59 qcm

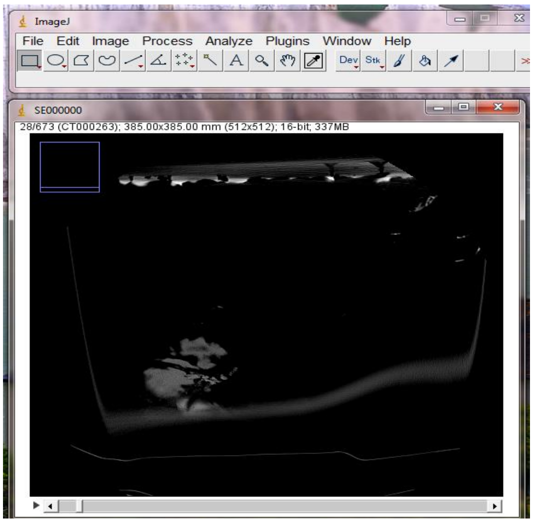


Figure 5.2a

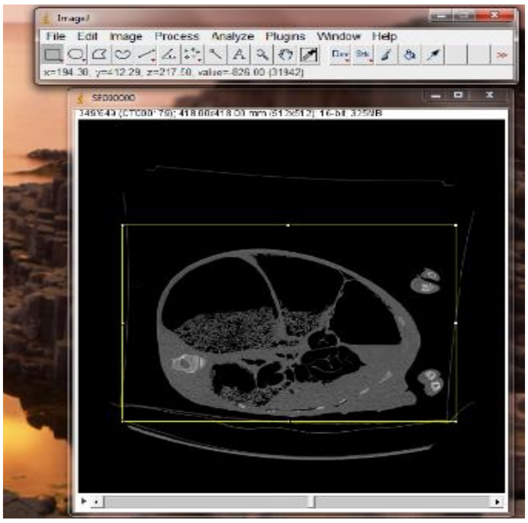


Figure 5.2b

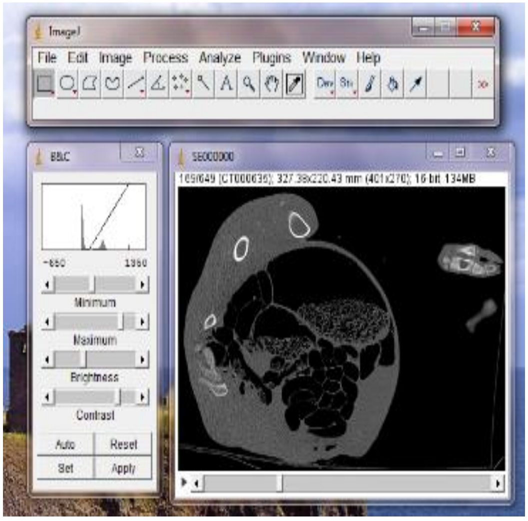


Figure 5.2 c

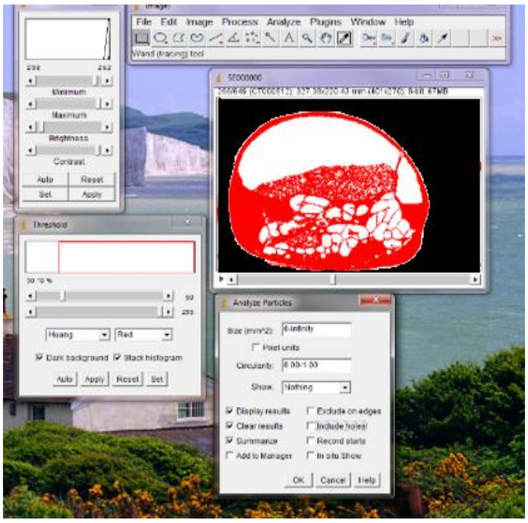


Figure 5.2 d

Figure 5-2. Shows the steps followed to calculate total body air volume using ImageJ software

5.1.4 Results

Tissue density

Although the time interval before changes became manifest varied for the different organs, overall there was a significant decrease in organ HU with increasing PMI. Conversely, the soft tissues surrounding the hip and shoulder joints and the kidneys showed an increase in HU with time. These changes are summarised in (Table 5-1, Page 120) and (Figure 5.3, Page 119).

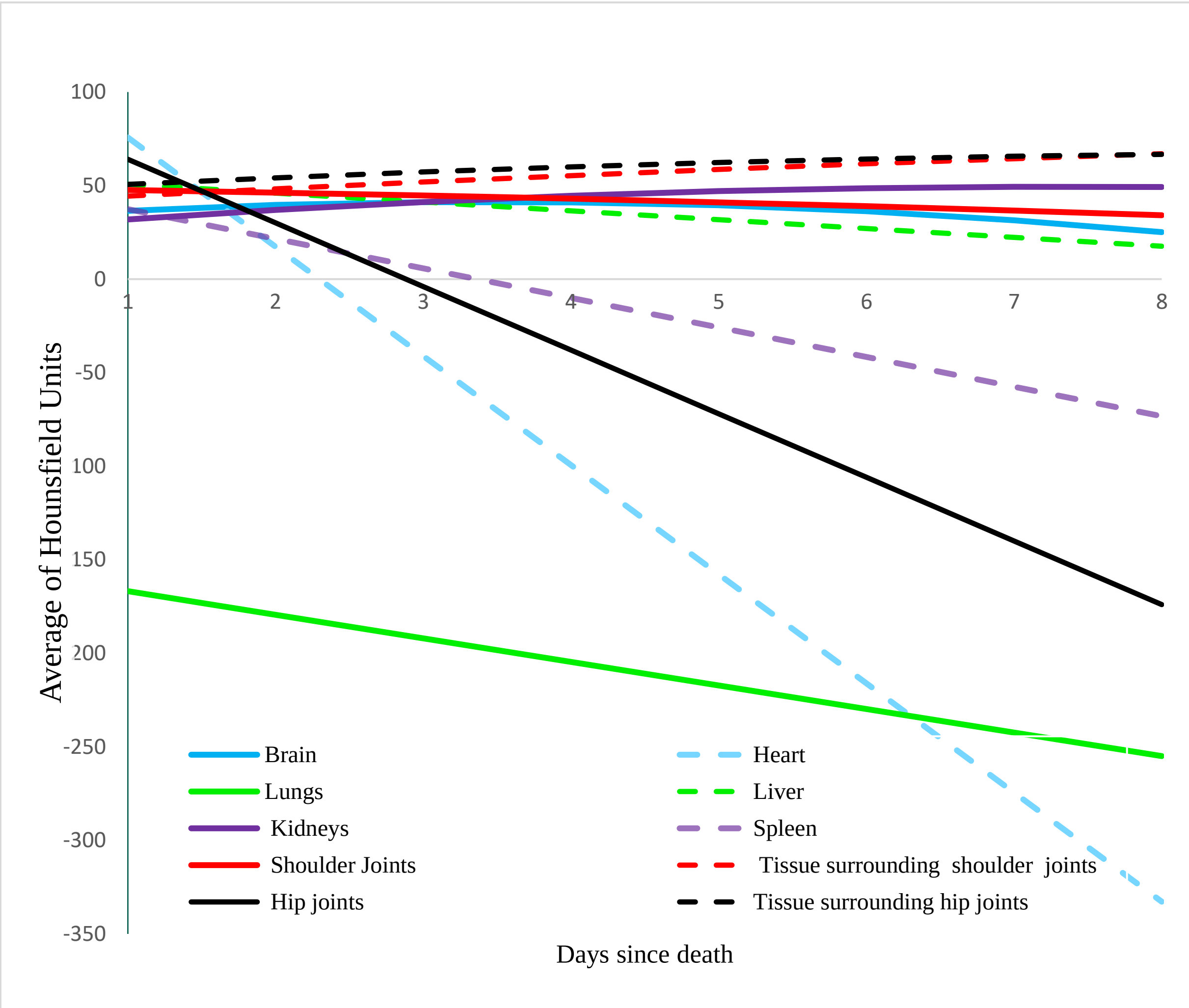


Figure 5-3. Graph showing change in HU of various tissues and organs in the first 160 h after death

Table 5-1. Change in organ HU over time

Organ	Time before significant change in HU (Hours)	Average Hounsfield Unit (HU) for each day 1	2	3	4	5	6	7	Rate of decrease per day	p value	Intercept	p value
Brain	72	34	37	44	-	34	-	27	0.4	0.414	37	0.001
Heart	16	44	51	54	-	-270	-	-289	58	0.001	76	0.001
Hips–joints	16	47	47	48	-	-147	-	-141	34	<0.001	62	<0.001
Hips–soft tissue	16	47	52	56	-	61	-	65	3	<0.001	51	<0.001
Kidneys	16	31	33	41	-	45	-	48	3	<0.001	37	<0.001
Liver	16	51	47	36	-	27	-	21	5	<0.001	51	<0.001
Lung	16	-145	-156	-227	-	-226	-	-245	13	0.002	-167	0.002
Shoulders–joints	16	48	47	44	-	40	-	35	2	<0.001	48	<0.001
Shoulders–soft tissues	16	46	53	55	-	61	-	66	4	0.015	43	<0.001
Spleen	16	45	44	-23	-	-34	-	-66	16	<0.001	37	<0.001

5.1.4.1 Air volume

PMCT scan images showed that decomposition of the lambs (as evidenced by gas formation) began in the heart, liver and stomach wall, was seen at the time of the first scan (from around 3 hours after death) and visibly increased until the last scan at approximately 160 hours. (Figure 5-4, Page 121) illustrates this process in the heart. Putrefaction air increased by (1696 mL + 395 mL / day) for each additional day after death, also TBAV / weight (51.325 mL/Kg/day + 231 mL/Kg). (Table 5.2, Page 122) and (Figure 5.5, Page 123) show the increase in TBAV / Weight (mL/Kg) for individual lambs and for each day following death. As can be seen, larger lambs had an increased TBAV ($p < 0.001$).

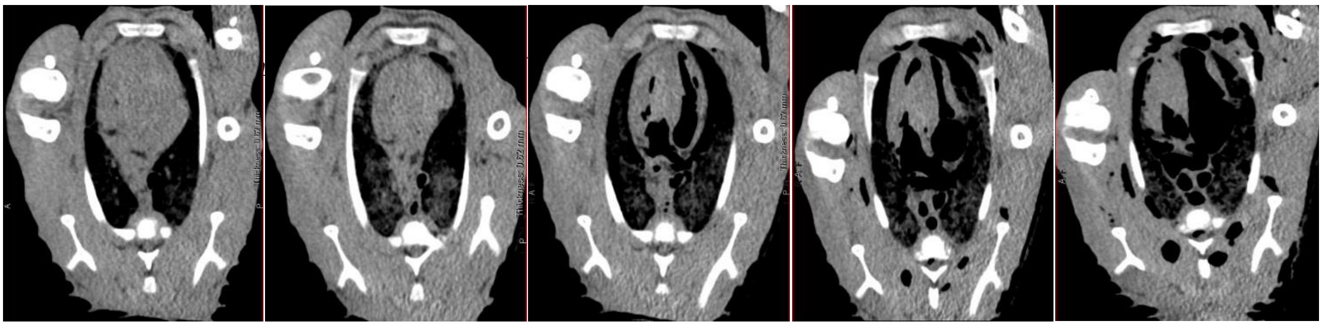
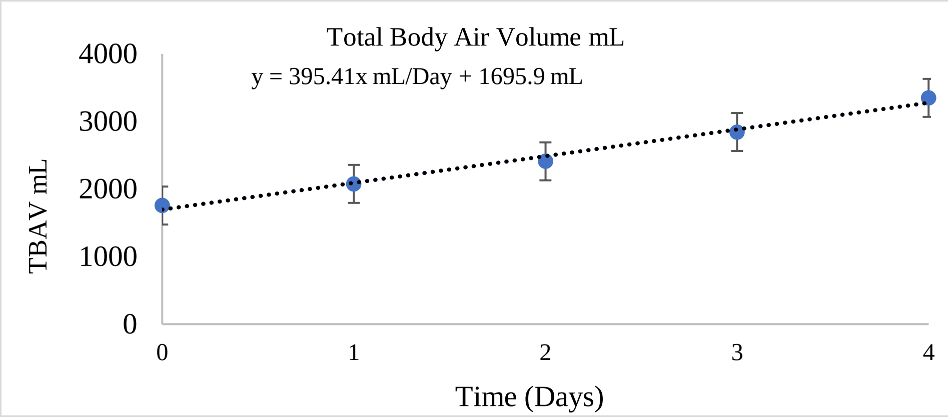


Figure 5-4. Shows Axial CT slices through the chest at the level of the ventricles in Lamb 5 (weight 7.55 kg) illustrating progressive decomposition of the heart with increasing intraventricular gas volume

Table 5-3. Increase in total body air volume over time.

Lamb weight Kg	**Lamb TBAV mL**				
6.60	3763	4006	4247	4769	5300
6.75	1706	1949	2193	2436	2977
7.35	1841	2084	2328	2868	3409
7.50	1695	1939	2192	2789	3330
7.55	1806	2171	2536	2900	3441
8.15	1147	1390	1634	2054	2595
8.71	1056	1597	2138	2382	2625
9.10	1030	1471	2011	2552	3112
Average	1755	2076	2410	2844	3348
	Lamb TBAV mL/Weight (Kg)				
6.60	570	607	643	722	803
6.75	253	289	325	360	441
7.35	250	283	316	390	463
7.50	226	258	292	372	444
7.55	239	287	335	384	456
8.15	141	171	200	252	318
8.71	121	183	245	273	301
9.10	113	162	221	280	342
6.60	570	607	643	723	803
Average	239	280	322	379	446



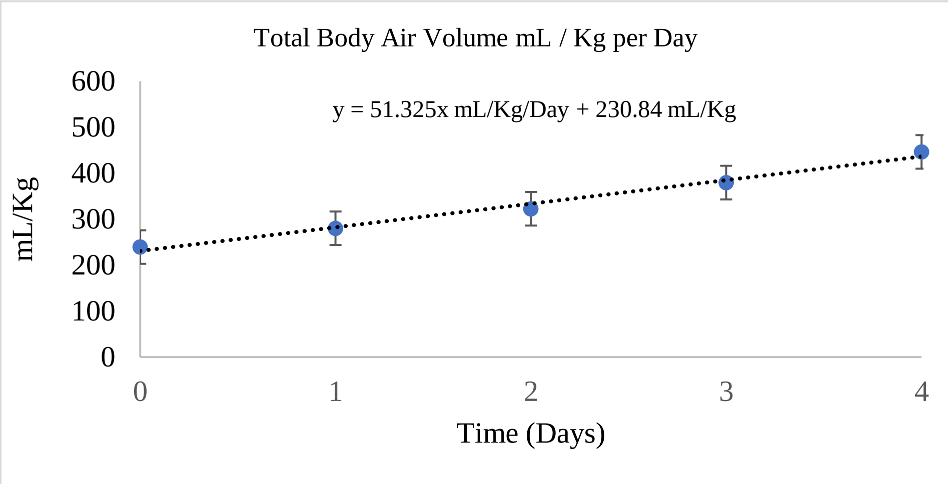


Figure 5-5. Total body air volume (mL) (top) and weight normalised total body air volume (ml/Kg) of each animal at 5 time points after death. Standard error bars and a linear fit are illustrated.

5.1.5 Discussion

With increasing emphasis on post-mortem imaging, we sought to assess the utility of PMCT for estimating PMI and showed measurable changes in HU and TBAV with increasing PMI. To our knowledge, the measurement of air volume to estimate post-mortem interval has not previously been reported.

Despite many years of research, accuracy in estimating the time since death has not significantly improved, and no single specific method can be used reliably (Swift, 2010). Immediately following death, a sequence of physical and chemical changes begins in the body (Lee Goff, 2009). Decomposition is a natural process that occurs in every organism after death. In the early stages decay might not be visible to the naked eye as the process starts at the cellular level. The process then moves to a macroscopic level and results in different post mortem changes (Fenoglio et al., 2010). Current estimates of the date of death are based upon a combination of observations made of the body and the scene of death. Observed conditions involving the body include rigor, livor, algor mortis and decomposition. The environment also plays an important role in the process of putrefaction and affects the levels of electrolytes and other biochemical factors in post-mortem samples.(Dix and Graham, 1999). Changes occur with differing degrees of constancy with regards to the order of their progress, and their rate is subject to an array of circumstantial and environmental factors. As a result of the variability, different stages of putrefaction can be observed on the same body simultaneously (Adlam and Simmons, 2007) and changes in the putrefaction process can considerably alter the estimate of the time of death (Campobasso et al., 2001). All of this makes estimation of PMI difficult and the development of more precise methods would be beneficial.

Concerning PMI and HU, we showed three patterns of change: initial insignificant increase in HU followed by an insignificant negative correlation in the brain;

immediate and continued decrease in HU in heart, lung, liver, spleen and hip and shoulder joints; and immediate and continued increase in HU for kidneys and tissues surrounding the hip and shoulder joints.

Initially in the brain there was a slight increase in HU (peaking at 16 hours and sustained for 3 days), following which there was a non-significant decrease in HU in all subsequent scans. Wang et al. (2017) showed similar results for the brain tissue of rabbits, in that HU were unchanged for the first 27 hours following death. This was followed by a phase of increasing HU, but then with increasing decomposition, air volume increased, and the HU of these areas gradually declined (Wang et al., 2017). The changes seen may be due to factors inherent to the cellular composition of brain tissue, such as glial cell swelling, neuronal karyopyknosis, Nissl degeneration and loss of white matter water content.

Heart, lung, liver and spleen showed a decrease in HU between the first and all subsequent scans up to and including the last scan at approximately 160 hours after death. Compared to the brain, this may be due to the higher rate of protein denaturation, water loss and/or loss of enzymes in the heart, liver and spleen as a result of blood stoppage in the early period after death. An increase in body temperature due to the chemical reactions in the body whilst being stored at 19^{o}C is another possibility but would not account for the difference in behaviour of the brain. The results of this study for the heart and lung are different to those of Wang et al (2017), who showed an increase in HU of these organs in the first two days after death (Wang et al., 2017). The reasons for this difference between the results of this study and Wang's study on rabbits are uncertain, but may be related to the differences in the anatomy of the animal species used. Lambs are larger than rabbits and we chose them to closer reflect the size of a human infant, but their digestive system is different to that of both humans and rabbits. At this age, the ruminant stomach of the lamb is not yet fully adapted to digestion of a vegetable diet but diverts milk directly into the abomasum, which is the chamber in the ruminant stomach most like a human monogastric stomach. For this reason it is reasonable to be cautious about the changes seen in the abdominal viscera, but we believe that the other changes we have recorded are likely to be closer to those in humans than to those in rabbits.

HU of kidney and soft tissues surrounding the shoulder and hip joints showed an increase between the first and all subsequent scans up to and including the last scan at approximately 160 hours. This might relate to the presence of amino acids in kidney tissue and muscles caused by tissue breakdown and to the presence of oedema or due to titin and nebulin in muscle tissue and deoxyribonucleic acid in the kidneys. Scarpelli et al (1990) stated that the onset of decay was rapid in tissue with a high content of hydrolytic enzymes, while it was intermediate in organs such as the kidney (Scarpelli, 1990). Ebuehi et al (2015) mentioned that degeneration was slow in intact nuclear DNA in the kidney and brain tissues with rising PMI (Ebuehi et al., 2015). Tomita et al. (2004) highlighted that skeletal muscle is the most abundant in the body and has a much greater delay in degradation compared to kidney, pancreas, liver and heart tissues after death which will clearly affect estimation of PMI (Tomita et al., 2004).

On the first scan, putrefaction was not significant, although pockets of gas could be seen in heart, liver and stomach wall. By the time of the second scan, PMCT images showed the presence of air in the blood vessels. From the third scan onwards, the areas of decomposition and the volume of air visibly increased throughout the body. By the time of the final scan the body organs had started to decay. This is due to bacteria and fungi which are the prime cause of decomposition (followed by chemical decomposition). Distention is usually most notable in the abdomen and later in the bulging of the eyes, but can occur in all soft tissues, and often develops at approximately 60 to 72 hours after death in humans. It may however occur significantly faster or slower depending on environmental conditions (Munro and Munro, 2008).

The average increase in TBAV was (51.325 ml/Kg/day + 231 mL/Kg) and a change of (395.4 ml/day + 1696 mL) per day. There was some overlap between TBAV of individual lambs; this was due to a significant difference in TBAV of three out of the eight lambs. Values were similar for the remaining five lambs. This may be due to differences in body size of these lambs (two of the three outlier lambs were of larger weight than the other six). Previous authors have pointed out that corpse size influences the rate of tissue degradation, with larger corpses decaying faster (Matuszewski et al., 2014). A further explanation may be the time interval between feeding and death as it is recognised that chemical reactions to food in the stomach may increase bowel gas (Vass et al., 2002). We did not record the time of the last feed in the studied lambs. A further limitation of this study is that although all lambs were stored at room temperature, this was not controlled, so there may have been alterations in ambient temperature due in part to different weather conditions for the 3 groups (scans were performed in the period between 11th April to 2nd May 2017). Assessing the effects of altered environmental parameters would provide still greater insights into the use of non-invasive PMCT to accurately determine PMI. In this study, only one reader measured the HU from six sites and TBAV which can be added to the limitations of this study. Also, the animal was not weighed prior to each scan which may have affected the results.

5.1.6 Conclusion

Results from this study suggest that measuring post-mortem tissue density has potential to be used as a non-invasive method to estimate time of death. However, there was variation in the behaviour of tissues from different organs. These differences are likely related to the characteristics of different organs and the different types and content of the enzymes present. Although TBAV showed significant correlation between PMI, there was also significant overlap between individual animals. Anatomical differences (e.g. size differences) and variable temperature and humidity almost certainly influence the rate of change and therefore should be considered in future larger studies. Combining HU of multiple organs and TBAV as a single index may prove more accurate than measuring the individual parameters and should be considered in any validation studies. With further research, PMCT may be developed to determine PMI in humans.

6. Chapter Six

6.1 **Estimation of Time of Death in Children Using Post-Mortem CT**

6.1.1 Abstract

Background

Estimation of time of death informs clinical-pathological correlations and is crucial in forensic investigations. Most studies have estimated time of death using forensic entomology and/or acarology. These methods only apply after decomposition has begun and although they indicate the minimum post-mortem interval (PMI) or time since death, their precision is limited.

Determination of Hounsfield unit (HU) is a useful clinical application of computed tomography (CT) scans when the nature of an abnormal finding is in doubt. The HU which is based on the attenuation of the x-ray beam in tissue which itself depends on the composition of the tissue and thickness of the anatomy passed by the beam (water is 0 HU and air is −1000 HU). The study done by Wong (2017) has suggested more research is required using HU. CT scan has HU,

Purpose

To determine whether post-mortem CT (PMCT) can be used to estimate post mortem interval (PMI) in children through the measurment of Hounsfield units (HU) of selected organs.

Methods

Measurements were taken of HU of the brain, heart, lungs, liver, kidneys and spleen from PMCT scans of 51 infants and children. Second order polynomial regression was used to assess the changes in HU with respect to time.

Ethical approval

Ethical approval for this study was obtained from the Health Research Authority (SCH/15/064).

Results

Of the 51 infants and children, 32 (63%) were male. The linear trends were significant for kidney, spleen, liver and brain for time between death and PMCT (p= <0.001), (p= <0.001), (P= .001) and p= 0.698) respectively. The estimated decrease in HU of kidney, spleen and liver was 0.047, 0.044 and 0.044 per hour respectively. However, it should be noted that the quadratic term was also significant for kidney and spleen (p= 0.015 and 0.028 respectively), indicating significant changes in rate of decay with respect to time for these organs.

Conclusion

This pilot study indicates that further investigation into the HU of kidney and spleen of humans may enable the creation of a method for assessing post-mortem interval.

6.1.2 Introduction

Estimation of time of death informs clinical-pathological correlation and may be crucial in forensic investigations (Buchan and Anderson, 2001). Most studies have estimated time of death using forensic entomology and/or acarology. These methods only apply after decomposition has begun and although they indicate the minimum post-mortem interval (PMI) or time since death, they are limited in their precision (Lee Goff, 2009). Myburgh et al. (2011) used accumulated degree days (ADDs) for determining PMI by taking the sum of the average daily temperatures for the length of time the cadaver had been decomposing. Several physicochemical processes start within the corpse after death and the resulting changes from these processes occur in a predictable order (Myburgh et al., 2013). The length of each stage and the overall velocity of decomposition will be influenced by different factors such as temperature, humidity, age of the deceased, whether the individual was using certain medications or if the cause of death was related to an infection (Buchan and Anderson, 2001, Vass et al., 2002, Gill-King, 1997) . The velocity of chemical reactions increases two or more times with each 10°C rise in temperature as defined by the physical principle known as Van’t Hoff’s rule, or the rule of ten (Gill-King, 1997, Knight, 1997).

A considerable number of studies have been performed using animal subjects but available data on PMI in human cases is limited [1]. An obstacle in the interpretation of the animal data is the significantly different research methods used and species studied, making it hard for researchers to provide general conclusions (Brooks, 2016). In humans, research on PMI has been conducted using both case-based studies and controlled studies with victims.

Post-mortem computed tomography and magnetic resonance imaging (PMCT and PMMRI) are increasingly being used in forensic examinations (Heng et al., 2009). CT scans allow the measurement of Hounsfield units (HU), where HU is the attenuation of the x-ray beam in tissue and depends on the composition of the tissue and thickness of the anatomy passed through by the beam (Lamba et al., 2014). The measurement is used to characterise different tissue types in the body (Levi et al., 1982) and has been used for several decades. Zech et al (2014) stated that in PMCT images of fresh corpses, serous fluids and blood can be considered and differentiated based on the ranges of their HU values. The HU value ranges of decomposition fluids overlap with those of serous fluids and blood in fresh corpses. Using Different beam energies and corpse temperatures had only minor effect on the HU value ranges and therefore should not complicate the differentiation and characterization of body fluids and blood (Zech et al., 2014). Also, the study in 2012 showed that in long-term PMCT examinations no significant amount of gas was detected within the intrahepatic arteries (Fischer et al., 2012). Despite this, only a limited number of studies (in animals) have used HU from PMCT scans to determine time since death, including Wang et al (2017) who used the technique in dead rabbits. The present study aims to determine the relationship between HU of selected organs and PMI in children. To our knowledge, this study is the first to correlate changes in HU of different six organs in children with post-mortem interval.

6.1.3 Study Design

6.1.3.1 Methods

PMCT scans were performed in two batches between 21st February 2012 and 24th November 2014 (n = 31) and between 13th October 2016 and 5th December 2017 (n = 20). All bodies were stored in a mortuary at 4 °C prior to PM imaging. The PMCT images were reconstructed and reformatted, HU was measured from serial PMCT images using the Radiology Department PACS system, and the average HU calculated from values recorded at six sites in each organ. A single observer performed all HU readings. The time of death for each case was recorded from the post-mortem report and the researcher recorded the exact time of PMCT from the workstation of the CT scan. It should be noted that the time of death recorded in the PM report was not an exact time in all cases due to some cases being the time of post mortem and some the last time the child was last seen alive.

6.1.3.2 Image acquisition

All PMCT examinations were performed at Sheffield Children's Hospital, by a trained radiographer, using a Lightspeed VCT 64-slice helical CT scanner and standard scanning parameters of 100Kv and 60 mA for chest, abdomen and pelvis, and 120Kv 300 mA for brain; 0.625 mm contiguous axial slices were obtained and images reconstructed with soft tissue and bone algorithms to provide 5 mm and 1.25 mm thick slices. The total time taken for PMCT image acquisition was less than 5 minutes and images were viewed on a standard soft tissue window. The scans were reformatted and HU were recorded at six sites from the brain, heart, lungs, liver, spleen and kidneys. All HU were measured by a single researcher using the Radiology Department PACS system at Sheffield Children's Hospital.

6.1.3.3 Ethical approval

The ethical approval for this research was obtained from the Health Research Authority (Reference Number SCH/15/064).

6.1.3.4 Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 24 for PC (IBM Corp, Armonk, NY). Polynomial regression was used in a stepwise fashion; initially a simple linear regression was performed to assess trends HU with time and in the second step a quadratic term was added to assess whether there was systematic deviation from the trend.

6.1.4 Results

This study measured HU from PMCT scans of fifty-one children. HU were measured for brain (a), heart (b), lungs (c), liver (d), kidneys (e) and spleen (f) in 41scans; from heart, lungs, liver, kidneys and spleen of 4 scans; and from the brain in only 6 scans (Table 6-1, Page 135 and Figure 6-1, Page 136).

Table 6-1. Shows the demographics of cases and average of Hounsfield units, which were measured from different tissues.

	N	Minimum	Maximum	Mean	Std. Deviation
Age (years)	51	.00	15	2	4.4
Estimated time from death to PMCT (Hours)	51	7	2144	96	297
	Average HU as measured from different organs				
Organ	**Minimum**		**Maximum**	**Mean**	**Std. Deviation**
Brain	-309		42	27	50
Heart	-23		56	46.9	12
Lungs	-724		52	-225	204
Liver	19		63	54	6.9
Kidney	15		45	38.4	4.7
Spleen	24		61	53.6	5.5

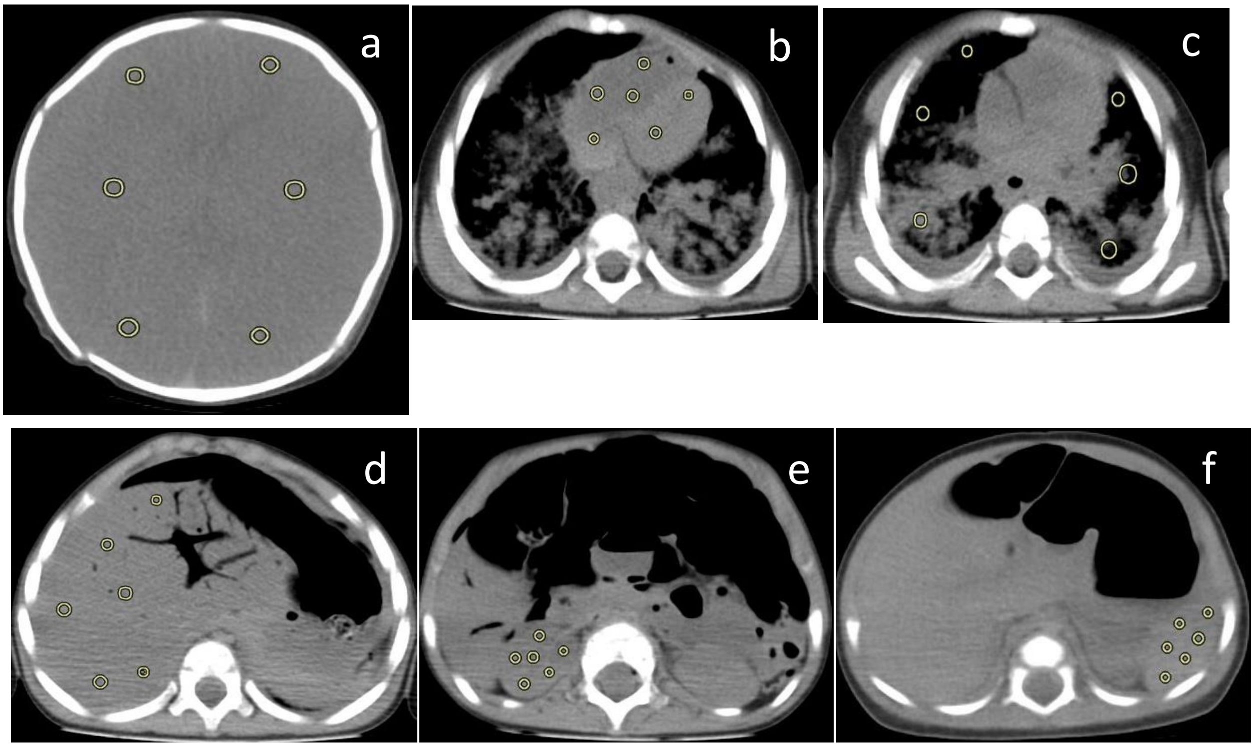


Figure 6-1. Shows the evaluation of radiopacity changes of different organs tissue six regions of interest (ROI) used PACS within each organ as shown in this image. ROI 1: area ≤ 0.59 qcm

6.1.4.1 Polynomial Regression Analysis

The HU of different organs measured from PMCT scan images showed significant changes dependent on the time since death.

Kidney:

The linear trend (-0.047, Std. Error = 0.008) in HU of the kidney with time was significant (p= <0.001). The estimated rate of change of HU of the kidney was 0.047 per hour. However, it should be noted that the quadratic term was significant (p= 0.015) implying that the rate of change varies with time (see Figure 6.2, Page 137).

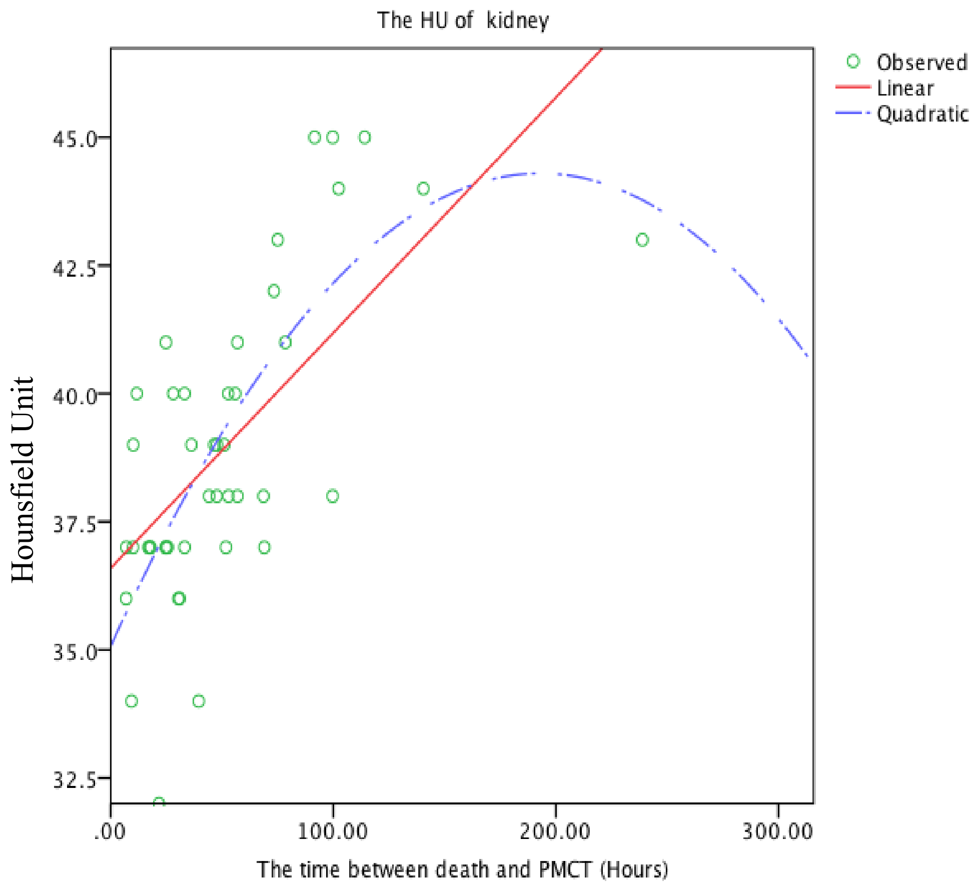


Fig 6-2. Graph showing change in HU of kidney with increasing time between death and PMCT

Spleen:

The linear trend (-0.044, Std. Error =0.009) in HU of spleen with time was significant ($p = <0.001$). The estimated rate of changes of HU of the spleen was 0.044 per hour. However, it should be noted that the quadratic term was significant ($p = 0.028$) implying that the rate of change varies with time (see Figure 6.3, Page 138).

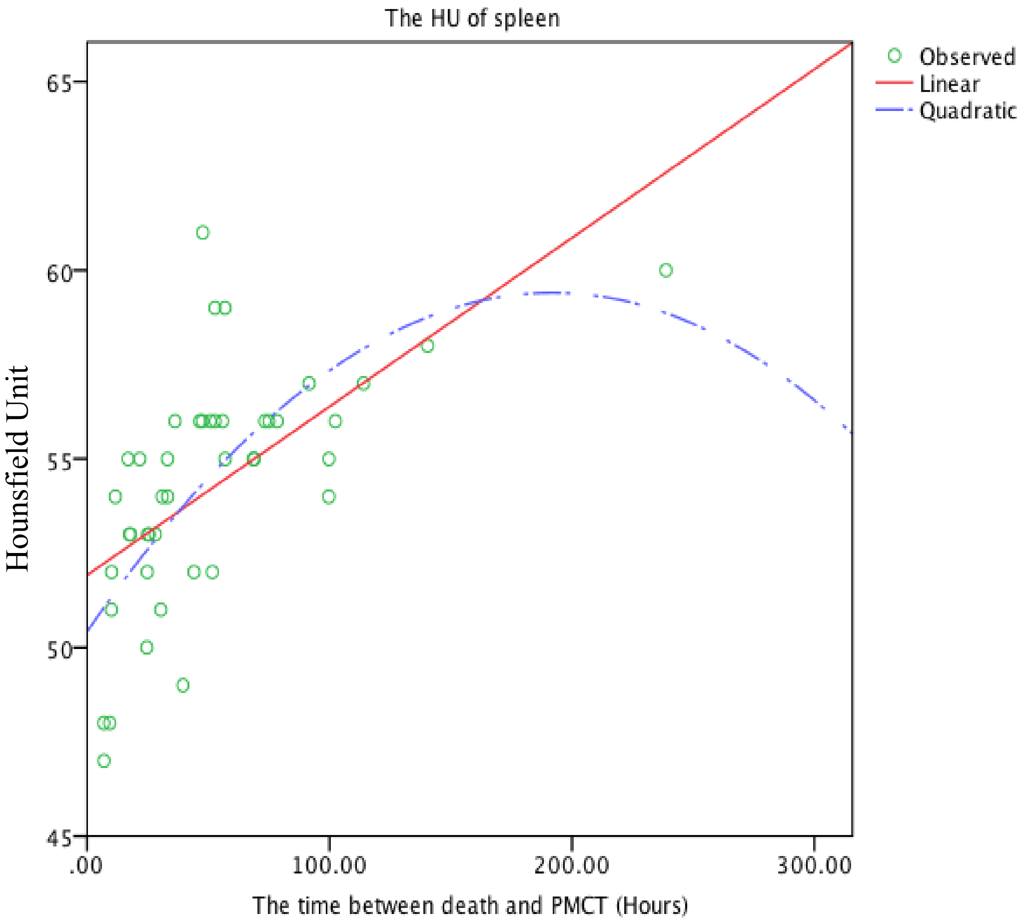


Fig 6-3. Graph showing change in HU of spleen with increasing time between death and PMCT

Liver:

The linear trend (-0.051, Std. Error =0.014) in HU of the liver with time was significant ($p= 0.001$). The estimated rate of changes of HU of the liver was 0.050 per hour. However, it should be noted that the quadratic term was not significant ($p= 0.544$) (see Figure 6.4, Page 139) and therefore the rate of change with respect to time may be considered constant.

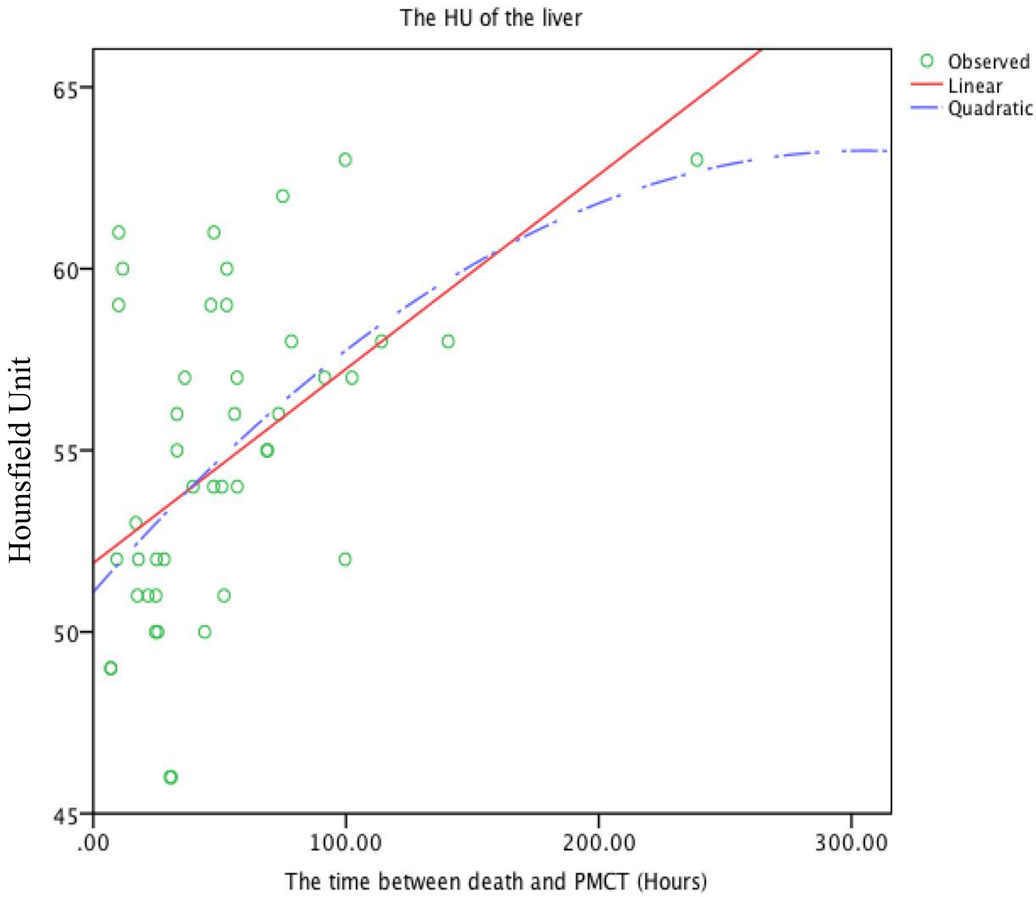


Fig 6-4. Graph showing change in HU of liver with increasing time between death and PMCT

Brain:

The linear trend (-0.004, Std. Error =0.10) in HU of the brain with time was not significant (p= 0.698). However, it should be noted that the quadratic term was also not significant (p= 0.873) and there is no discernible pattern with respect of HU to PMCT for the brain (see Figure 6.5, Page 140).

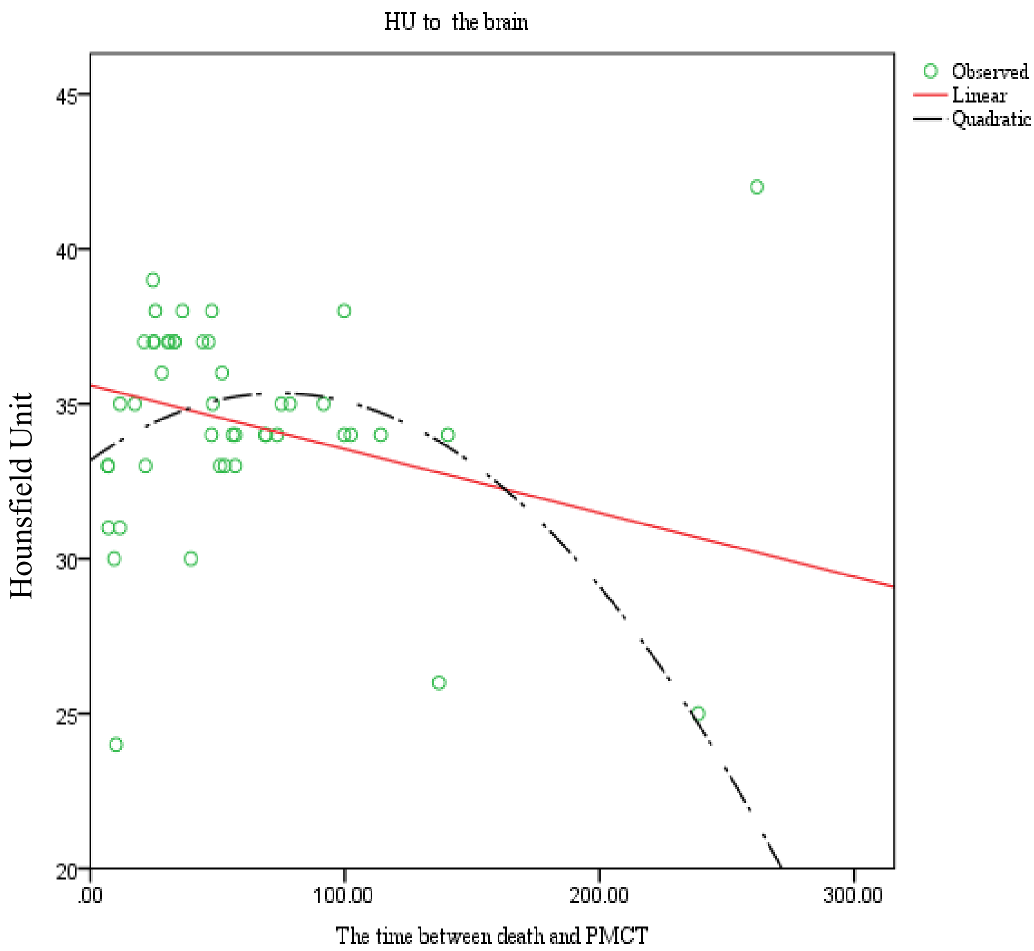


Fig 6-5. Graph showing change in HU of brain with increasing time between death and PMCT

Heart:

The linear trend (-0.01, Std. Error = 0.02) in HU of the heart with time was not significant (p= 0.23). However, it should be noted that the quadratic term was also not significant (p= 0.747) and hence there is no discernible pattern with respect of HU to PMCT for the heart (see Figure 6.6, Page 141).

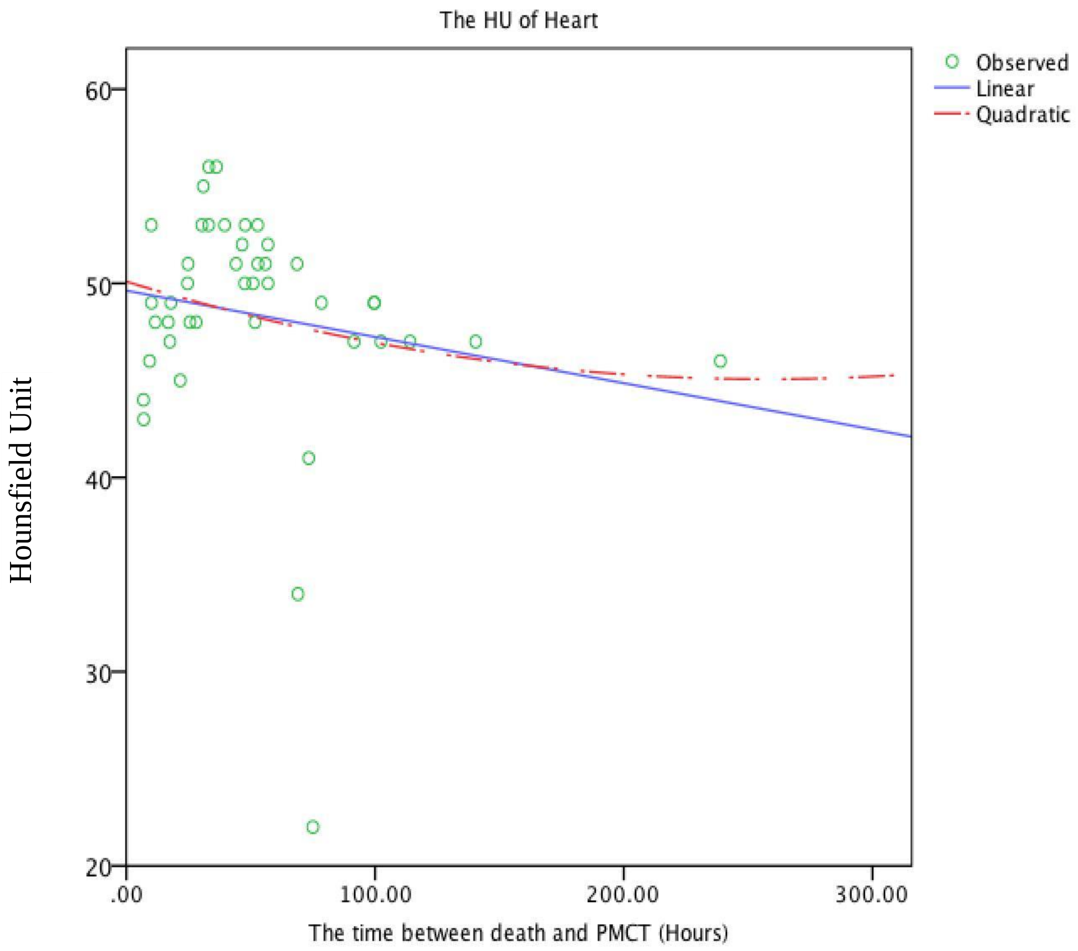


Fig 6-6. Graph showing change in HU of heart with increasing time between death and PMCT

Lungs:

The linear trend (-0.018, Std. Error = 0.73) in HU of the lung with time was not significant (p= 0.623). However, it should be noted that the quadratic term was also not significant (p= 0.327) and hence there is no discernible pattern of change with respect of HU to PMCT for the lungs (see Figure 6.7, Page 142).

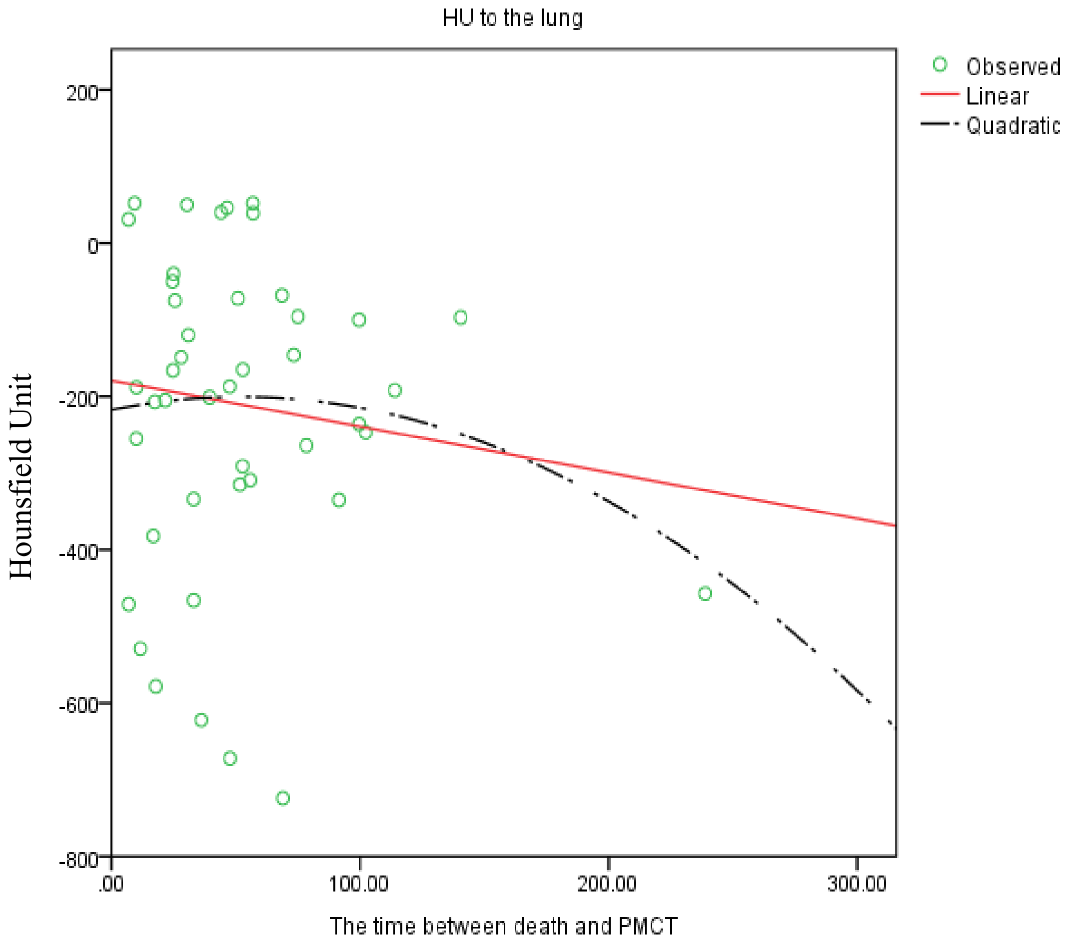


Fig 6-7. Graph showing change in HU of lung with increasing time between death and PMCT

6.1.5 Discussion

In Children, estimating post-mortem interval has been widely study from a clinical-pathological prospect. However, studies form radiological prospect is limited. To our knowledge, no previous study correlated changes in HU of organs in children with post-mortem interval. In light of the absence of such as study, this study measure the change of HU in different six organs to estimate the post-mortem interval. Of the HU numbers measured, our results indicate that the kidney provides the most accurate prediction of time elapsed since death. The study showed that a significant increase in the kidney HU occurs within the first 300 hours after death. However, the quadratic term indicated that subjects whose PMCT was performed more than 200 hours after death have markedly lower HU numbers than would be expected from the straight line. This result is supported by a study done recently which showed that the HU in the kidney of lambs was increased in all scans until the last scan at approximately 160 hours (Ben Taher, 2018). Vass et al. (2002) also pointed out that renal tissue is considered an important tissue to estimate PMI using cumulative degree hours (CDH) (which uses a twelve-hour temperature cycle to explain the decomposition process).

This study showed significant increases in the linear trend in the HU of spleen and liver tissue up to 300 hours. Furthermore, the quadratic term showed a significant increase in the HU of spleen tissue within approximately 200 hours following death. In our study, the quadratic equation for the liver showed no decrease up to 300 hours after death. However, for both liver and spleen, the single point over 200 hours was lower than would be expected for a linear curve. The statistical analysis showed that there is a negative correlation between the HU of spleen and liver tissue which changes with time. This may be due to the liver and spleen having different rates of protein denaturation and water and enzyme loss at different points in time after death. In addition, differences may be due to storage of the body in a fridge at 4^{o}C or due to the variation in age of (0 to 15 years), which might affect the speed of the chemical reactions in the body of the victim. Environmental factors such as humidity, temperature, age, body size of the deceased, disease/injures and use of medication can influence estimation of time of death (Gill-King, 1997, Buchan and Anderson, 2001, Mann et al., 1990) in spite of all decomposing bodies going through the same decomposition stages (Gill-King, 1997). Vass et al. (2002) stated that liver tissue is one of the most useful PMI indicators for early putrefaction. While changes in HU occurred, PMCT images did not show clear decomposition presumably due to the bodies being refrigerated.

In this study, brain tissue did not prove important for determining PMI. The linear trend showed a decrease in the HU of brain tissue from approximately 0 hours until over 300 hours after death. However, the quadratic term initially showed increases in HU but were followed by a decrease at approximately 290 hours, with the highest value reached within 100 hours after death. These changes may be due to the fact that the brain tissue consists of white matter, grey matter and a large amount of water. Our results are supported by Ben Taher et al (2018) who found that the change in HU of brain tissue in lambs at the beginning was slightly increased (peaking at 16 hours) and was sustained for 3 days after that period. The HU then decreased in all subsequent CT scans. Vass et al. (2002) stated that it is important to use brain tissue in early cumulative degree hour (CDH) ranges, however, it has limited use for determining long-term PMI determinations since the effective CDH range only extends to approximately 270 CDHs (Vass et al., 2002). Also, Wang et al. (2017) demonstrated that the brain tissues of rabbits were unchanged during 0–27 hours after death. With increasing decomposition, the HU of brain area continued to gradually decline and the putrefaction started to appear in the base and middle of skull 27 hours after death. Wang et al. also demonstrated that the average HU of rabbit brain tissue decreased during the first 5 days after death. The overall trend was for a decline in values but values were seen to increase first and decrease later; the highest value of HU reached at 33 hours after death (Wang et al., 2017).

In this study, both the linear and quadratic trends showed that the HU of lung and heart tissue showed no clear pattern with time. Also, PMCT images did not show clear decomposition changes within the period analysed after death. This may be due to the lung and heart having different tissue composition and to the presence of air in the lung. In the future, we suggest that comprehensive analyses of several indicators of different organs may establish a method to overcome the deficiencies of each and make the estimation of PMI more useful and scientific.

6.1.6 Conclusion

This study indicates that the HU of the kidney and spleen in humans may enable the creation of a new method for assessing time since death. It showed however that HU values from the liver, brain, heart and lung tissue have limited use. The study also for estimating PMI and that further research is required studying larger populations and investigating combinations of techniques.

7. Chapter Seven

7.1 General Discussion and Future Work

The study presented in Chapter Two was the first to formally investigate the acceptability of PM CT and MRI to Libyan Muslims and UK Muslims of Libyan descent compared with that of non–Muslim UK residents. The questionnaire's response rate was 92% from Muslims and 69% from non-Muslims showing the importance given to this subject, particularly amongst Muslim respondents. The study showed that both Muslims and non-Muslims perceive conventional autopsy to have a negative emotional effect on family members due to its invasiveness and, for Muslims, it will lead to delay in burial.

The Islam religion requires burial of the body as soon after death as possible to reduce the emotional effect on the family and to respect the deceased. It is clearly demonstrated in this study that Muslim participants in Libya support this view, with a significant number feeling that burial should occur within 12 hours of death. In our study, there were a small number of Muslim participants who felt that medical imaging could lead to a delay in burial.

Muslim and non-Muslim participants in this study also believed that the dignity of the deceased can be preserved using medical imaging. On the other hand, non-Muslim participants were more willing to accept that a conventional autopsy would not infringe the body’s dignity and here, the effect of religion is clearly visible. This result was supported by other studies including 1) Lynch (1999), who mentioned that Hindus and those of other religions are believed to have a less intrinsic interception to an autopsy than Muslims (Lynch, 1999), 2) the Cox et al (2011) study which reported from Uganda that 59% of parents or relatives (Muslim and non-Muslim) looked unfavorably on autopsy for reasons including delayed burial, body mutilation and reasons of a religious nature. 3) Loughrey (2000) who found that parents may prefer to "maintain the physical dignity" of their loved one, rather than define the precise cause of death using an autopsy and 4) Parmar and Rathod (2013) who stated that most of the participants refused conventional autopsy due to the delay in burial and concern about the cutting of the body, removal or sale of organs.

Despite the overall preference for PM imaging over conventional autopsy, this study found that Muslim participants preferred conventional autopsy for the investigation of homicides and PM imaging for the investigation of unsuspicious deaths. Muslims' opinions would indicate more trust in the ability of conventional autopsy to explain the circumstances of suspicious death. Hussain et al (2006) showed that 78% of cases of homicide deaths were explained by conventional autopsy.

In Chapter Three, PMCT is shown to play an important role in identifying causes of death. This study provided percentages for identifying the abnormality using PMCT and autopsy from 11% to 74%.

This review showed that PMCT can detect fractures better than autopsy. The study done by Krentz et al. (2016) showed that PMCT identified multiple skull fractures, a small fracture of the occipital bone and fractures of the right temporomandibular joint, whilst facial and temporomandibular fractures were not reported by autopsy. Furthermore, PMCT may detect some brain abnormalities (such as subdural hematoma), small pneumothoraces or haemothorax and brain oedema which could be difficult to identify on autopsy (Krentz et al., 2016, Kawasumi et al., 2015).

PMCT can provide more information to the pathologist prior to the start of the autopsy by showing the body’s anatomy. For example, PMCT could be used to highlight when there is a need to investigate and identify the location of fractures (Krentz et al., 2016).

In Chapter Four, the study of PMCT showed that, in general, it is superior to autopsy for identifying fractures. This particularly for fractures which may be difficult to detect by autopsy, such as proximal phalanx left thumb or in pelvic fractures such as ischium and pubic fractures. Our results are supported by a study in 2013 which found that an autopsy may not detect the bone abnormalities in different regions in the body, particularly in the areas which are not routinely investigated by autopsies, such as some pelvic or facial bones (Christine et al., 2013). PMCT has the ability to provide important information regarding trauma that may be not identified on conventional autopsy.

Other studies have identified that PMCT can be used to detect suspected inflicted injury, especially when rib fractures or brain injury are involved (Dedouit et al., 2008b, Dedouit et al., 2008a). This study showed in cases of death related to trauma (e.g. Cases 48 and 49) that PMCT identified multiple fractures of the skull, ribs, pelvis and lower limbs. However, the study suggested that PMCT had less sensitivity than autopsy to detect overall abnormalities in different body systems or organs. Grabherr et al. (2018) stated that combining both post-mortem imaging techniques and autopsy can increase the quality of explaining the abnormality of post-mortem cases in soft tissue and organs' parenchyma. Although the detection of abnormalities of the parenchymal and soft tissue using PMCT shows less than the ability of PMCT to detect bone fractures, this may also be improved by combining PMCT angiography and autopsy, for instance to detect pneumonia and identifying soft tissue injuries. PMCT without contrast agent could not differentiate ante-mortem pulmonary lesions that might be due to other causes of death, (e.g. aspiration pneumonia, infection and cardiac failure), from post-mortem changes and/or non-specific findings (including pulmonary oedema, pulmonary atelectasis and congestion). There could also be a contradiction between conventional autopsy and PMCT if the cause of death is pneumonia (Noda et al., 2013).

PMCT imaging has improved in the forensic field especially in adults and recently the research increased conducted to evaluate the agreement between PMCT and conventional autopsy in childhood. For that, the radiologists should have more expert with non-specific post-mortem changes in order to differentiate these changes from specific signs which could explain the circumstances of death. Interpretations of PMCT images is subject to experience and a 'learning curve' and it is possible that the differences in percentage agreement may reduce as more experience is gained using PMCT. Previous studies have also suggested that forensic training for radiologists may improve their skills (Aghayev et al., 2008, Yen et al., 2007).

In Chapter Five, we sought to evaluate the utility of PMCT to estimate post mortem interval (PMI) and presented measurable changes in total body air volume (TBAV) and Hounsfield unit (HU) with increasing PMI. To our knowledge, the measurement of air volume to estimate post-mortem interval has not previously been used.

This study showed a negative correlation between the HU of lamb brain tissue and PMI. There was a slight increase in HU during the first three days after death, followed by a non-significant decrease in HU in all scans after three days until the last scan at approximately 160 hours following death. These changes may have been due to factors inherent to the cellular composition of the brain tissue such as loss of white matter water content, glial cells swelling, neuronal karyopyknosis and Nissl degeneration. The study results were supported by Brooks et al. (2016) who explained that, as a consequence of bacterial decomposition, body cavities and internal organs frequently become swollen by gases. In addition, Wang et al. (2017) demonstrated a similar result to this study' result were the brain tissues of rabbits were unchanged within the first twenty-seven hours after death. With increasing putrefaction, the gas volume produced from decomposition and the HU of these areas continued to gradually decrease. Wang et al. also found that the average HU of rabbit' brain tissue approximately 5 days after death showed some negative relationship with PMI. The overall trend was for a decline in HU, but values of HU were seen to rise first and decrease later at around one and a half days after death, and the average HU decreased until approximately five days after death.

The changes seen in the brain were different to changes seen in other organs. Within the first 3 hours following death, the average of HU values for the heart tissue declined. The HU of the heart tissue density also declined after the second CT scan (approximately 16 hours after death). PMCT images showed low density in the heart tissue with the emergence of decomposition gases in the heart at approximately 16 hours after death. Then, the HU of the heart tissue rapidly decreased until the last scan 160 hours after death. This might be due to water loss and/or a lower rate of protein denaturation and/or a loss of enzymes in the heart as a consequence of blood stoppage in the early period following death.

The Wang et al study and this study have similar outcomes with both showing that there is a negative correlation between the HU of the heart tissue and PMI.

This study used the HU of the liver and spleen to provide the predicting values that can estimate PMI from the time of death until the disappearance of the liver tissue after 7 days. The area of the liver and spleen tissues gradually declined with the extension of PMI and the statistical analysis showed that there is negative correlation between the HU and liver and spleen tissues. The decrease of HU after death in these organs might be due to different rates of protein denaturation and loss of water and enzymes at different times after death. The first and second scans shown no significant changes but decreases in HU were seen in subsequent scans. This difference might be due to a change in liquid composition or there may be an increase in body temperature due to the chemical reactions in the body whilst being stored at 19^{o}C. Vass et al. (2002) mentioned that the liver may be one of the most important organs for estimated PMI. Wang et al. (2017) demonstrated that the average HU of liver tissue increased after death and reached the peak approximately one and a half days after death. After this, the HU values gradually reduced. After approximately five days following death, the ratio of liver tissue gradually decreased with the extension of PMI, and the statistical analysis showed that there was some negative correlation between the PMI and HU of this tissue (Wang et al., 2017).

PMCT showed, however, that the HU of kidney tissue increased from the second scan and until the last scan after seven days. Within approximately 160 hours after death, the area ratio of kidney gradually increased with the extension of PMI, and the statistical analysis showed that there is a negative correlation between the HU of kidney tissue and PMI. This might be due to the presence of amino acids in kidney tissue.

This study showed that the average increase in TBAV was (51.325 ml/Kg/day + 231 mL/Kg) and a change of (395.4 ml/day + 1696 mL) per day. On the first scan, decomposition was not significant, but the second scan showed gas accumulation in the blood vessels of the heart, liver and in the abdomen. From the third scan, the volume of air had increased in the whole-body as a consequence of an increase in the areas of decomposition in the body. At the final scan, it was clear that the body organs had started to decay. This may be related to bacteria and fungi which are the prime cause of decomposition (followed by chemical decomposition). Puffiness is usually primarily observed in the abdomen and later in the bulging of the eyes, but might occur in different soft tissues. It often develops at approximately 60 to 72 hours after death in humans. It may however occur significantly faster or slower depending on environmental conditions (Munro and Munro, 2008). This study showed overlap between TBAV of the individual lambs which was due to a considerable difference in TBAV of 3 of the 8 lambs. This might be due to the body size of those particular lambs, as two of the three outlier lambs were of larger weight than the other six. Previous studies have stated that corpse size affects the rate of tissue degradation, with larger bodies decaying faster (Matuszewski et al., 2014). Moreover, it may be due to the time interval between death and the last feeding as it is known that chemical reactions of food in the stomach increase bowel gas (Vass et al., 2002).

The study presented in Chapter Six showed that kidney tissue provides the most accurate prediction of the time elapsed since death, with a significant rise in linear trend in HU in the first 300 hours after death. However, the quadratic term indicated that subjects whose PMCT was performed more than 200 hours after death have markedly lower HU numbers than would be expected from the straight line. This result supported a study performed recently which showed that the HU in the kidney was increased in all scans until the last scan at approximately 160 hours (Ben Taher, 2018). Vass et al. (2002) pointed out that kidney tissue is considered an important tissue in estimating PMIs in the late period since death using cumulative degree hours (CDH) (which uses a twelve-hour temperature cycle to explain the decomposition process) (Vass et al., 2002).

This study showed a significant increase in the linear trend in the HU of liver and spleen tissue up to 300 hours after death whilst the quadratic term showed a significant increase in HU of the spleen tissues within 200 hours after death. The quadratic equation in this study showed no decrease up to 300 hours after death. However, both the liver and spleen showed stability at a point over 200 hours that was lower than would be expected for a linear curve. Statistical analysis identified a negative relationship between HU and changes in the tissues of the spleen and liver. This may be the result of malformation of the proteins and enzymes and loss of water in the liver and spleen at different periods of time after death. In addition, these differences may be related to storage of the body in a fridge at $4^{o}C$ which may affect the speed of the chemical reactions in the body after death. Despite all decomposing bodies going through the same decomposition stages (Gill-King, 1997), environmental factors such as temperature, humidity, the age of the deceased, disease and use of medication can influence the estimation of time of death (Gill-King, 1997, Buchan and Anderson, 2001, Mann et al., 1990). Vass et al. (2002) pointed out that liver tissue is considered one of the most important PMI indicators for early rotting and is an important instrument used to determine PMI. However, even though changes in HU occurred, PMCT images did not show clear decomposition within seven days after death.

7.2 **Limitations and Future work for five studies**

7.2.1 Limitations and Future work in Chapter two

Chapter two has been published in the British Journal of Radiology (BJR) (see page 71).

7.2.2 Limitations and Future work in Chapter three

One of the limitations in this study is the few numbers of studies, in which were most of them had low numbers of cases. However, we have no control over the number of the cases neither the studies. Additionally, restricting the search to those studies publish only in English may have also derived for lowered number of suitable studies for inclusion, however, the study has no funding to cover the cost of a translator. Furthermore, a meta-analysis would be preferred to affirm the conclusion of our systematic review, however, we found a significant heterogeneity amongst these studies which meant that it was not possible to perform meta-analysis. In our systematic review, PMCT without contrast agent showed limitations to detect the abnormalities in soft tissues or organ parenchyma. In future studies, it is recommended to use post-mortem angiography to identify parenchyma abnormalities.

7.2.3 Limitations and Future work in Chapter four

PMCT shows limitation in detecting chest abnormality compared to autopsy. Out of 34 cases, PMCT identified abnormalities in the chest in only 17 cases. One of the limitations is the poor resolution of the CT to identify the abnormalities in the soft tissue. Future work could evaluate the use of contrast in PMCT, to enhance the resolution of the CT images, which could aid the diagnosis. This study included two readers to compare the reliability between experts and non-experts readers in reporting PMCT. Our study included only one expert and one non-expert radiologists with regard to PMCT due to the limited time and resources to complete this project. Future studies will aim to include more experts and non-experts readers.

7.2.4 Limitations and Future work in Chapter five

Evaluation of the agreements between PMCT and autopsy and the use of post-mortem imaging for determining PMI in the forensic field needs large-scale prospective studies using animal and human tissue. The lambs in this study were stored at a room temperature that was not controlled. There may therefore have been alterations in ambient temperature, due in part to different weather conditions. Assessing the influences of environmental parameters could provide even greater insights into the use of non-invasive PMCT to accurately determine PMI. Never the less, more research studies are needed, including comparing this study with human studies to validate the results. As the time interval between death and the last feeding can affect the amount of gas in the bowel, future studies need to record the time of the last feeding before death. Also, future studies need to control for temperature during the storage period.

7.2.5 Limitations and Future work in Chapter six

This study demonstrated that there are some limitations, such as using a single indicator, for estimating PMI and that further research is required studying larger populations and investigating combinations of techniques. Another limitation is the use of one reader to measure the HU for the six organs in all of the infant, in which another reader would revealed more robust results, however, due to limited funding, the other reader was not included. Future research should include cases where the body has not been refrigerated immediately as temperature can affect the rate of decomposition.

7.3 Conclusion

Autopsy is the accepted gold standard for detecting cause of death, but its use has been in decline. Several studies in recent years have suggested that PMCT is useful for explaining the circumstances of death, particularly in trauma cases. However, PMCT cannot explain certain causes of death identifiable by autopsy such as cardiac disease, asphyxia and infection.

Various factors, such as religious beliefs and the age of the deceased, influence an individual's preference for post mortem investigation regardless of whether they are Muslim or non-Muslim. Muslim groups preferred medical imaging due to concerns that autopsy could lead to delayed burial. However, Muslims preferred conventional autopsy when the cause of death was suspicious. Muslims resident in the UK have an attitude closer to that of non-Muslims in the UK population. In conjunction with developing expertise in performing and reporting on PM imaging investigations and educational programmes, it may therefore be possible to change the attitudes of Muslims in Libya and other Muslims in different countries.

PMCT has limitations in detecting causes of death when compared to autopsy. However, PMCT has the ability to detect bone fractures, which may result from traffic accidents, blunt trauma or injury related to inflicted injures. Our results suggest that autopsy alone can no longer be regarded as the diagnostic gold standard for determining the cause of death; rather that a combination of autopsy and PM imaging techniques should be used, particularly for detecting the cause of death in traumatic cases. PMCT therefore should be considered an adjunct rather than an alternative to autopsy although a considerable number of prospective studies involving different circumstances of death are needed to further investigate both the complementary and/or replacement role of whole-body PMCT and PMMRI in infants and children.

PMCT may have a role in determining post-mortem interval, a fundamental task for the forensic pathologist who is consulted when the dead body is found. As a result of this study measuring HU from organ tissue, PMCT has the potential to be used as a non-invasive method for estimating PMI. Values of HU from the brain, heart and lung tissue have been shown to have limited use but further investigation into the use of the HU number of the kidney and spleen in humans might enable the creation of a method for estimating PMI.

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Appendices

7.4 Appendix I Public Perception Of Using Medical Imaging To Identify Causes Of Death Amongst The Libyan Community In Libya And Sheffield UK.

Background

The examination of a body after death to find out why somebody has died is termed post-mortem examination (PM). The traditional and gold standard method for this is autopsy, where body parts are opened up surgically and examined by specialists. An alternative method is conducting this examination using CT (computed tomography) or MRI (magnetic resonance imaging), which do not require the body to be surgically opened.

We are conducting a survey to assess the views and experience of Libyan resident in the UK, and Libyan and non-UK (Muslims/non-Muslims) resident in UK, regarding post-mortem examinations (either autopsy or CT/MRI).

By filling out and returning this questionnaire, you agree to us using your responses for the purposes of our research. We reassure you that it will not be possible for anyone to identify you from the answers that you give.

Thank you for your time in reading the information sheet and in considering whether or not to take part in this study.

Section 1:

About You

1. **Age (years):** __________

2. Occupation: ____

3. **Sex:**

Male ☐

Female ☐

4. Religion:

Muslim ☐

Christian ☐

Hindu ☐

None ☐

Other ☐ Please specify___________________

5. Ethnicity: ____

6. Country of origin:____

7. Highest qualification:

None ☐

University ☐

Secondary School ☐

Primary School ☐

8. Annual household income:

< £10600 ☐

£10601– £31000 ☐

£31001 - £785000 ☐

£785001 - £150000 ☐

> £150,000 ☐

Section 2:

Your Experience of PM (Autopsy, CT or MRI) Examination

1. Have you come across PM examination (autopsy) before?

Yes ☐ No ☐

2. Have you heard of PM examination by computed tomography (CT)

Yes ☐ No ☐

3. Have you heard of PM examination by magnetic resonance imaging (MRI)?

Yes ☐ No ☐

4. Do you know anyone (family, relative or friend) who had a PM?

Yes ☐ No ☐

5. If yes to Question 4, please complete the table below.

Cases	Age	Sex	When	Type of Autopsy		
				Conventional autopsy	CT scan	MRI
1.						
2.						
3.						
4.						
5.						

Section 3:

Your Views on PM Examination (Autopsy)

1. Performing PM examination leads to a delay in burial. What length of delay do you think is acceptable?

For An Adult:

< 12 hours ☐

12 – 24 hours ☐

1 - 3 days ☐

3 – 7 days ☐

> 1 week ☐

For A Child:

< 12 hours ☐

12 – 24 ☐

1- 3 days ☐

3 – 7 days ☐

> 1 week ☐

2. In general, which form of PM would you accept CT/MRI or conventional autopsy in the following situations:

   a. Homicide/suicide cases. CT ☐ MRI ☐ Autopsy ☐ None ☐

   b. Suspicious but natural deaths CT ☐ MRI ☐ Autopsy ☐ None ☐

   c. Natural, but unexplained deaths CT ☐ MRI ☐ Autopsy ☐ None ☐

   d. Natural and expected. CT ☐ MRI ☐ Autopsy ☐ None ☐

3. What concerns you about PM examinations?

   a. Delays in burial.

      CT ☐

      MRI ☐

      Autopsy ☐

      None ☐

   b. Dignity and sacredness of the body.

      CT ☐

      MRI ☐

      Autopsy ☐

      None ☐

   c. Emotional burden on the family.

      CT ☐

      MRI ☐

Autopsy ☐

None ☐

d. Cost effectiveness.

CT ☐

MRI ☐

Autopsy ☐

None ☐

Do you have other comments you would like to make or do you have any other anxieties about PM examinations?

....

....

Thank you for your time and cooperation. XXXXXX

PhD Student, University of Sheffield. If you have any questions, please do not hesitate to contact me on: XXXXXX

Or contact

Supervisor: XXXXX at the XXXXXX Telephone: XXXXX

7.5 Appendix II Autopsy protocol for sudden unexpected deaths in infancy

The role of the autopsy

To establish the cause of death and to address the issues related to the circumstances of death:

- whether the death is attributable to a natural disease process
- To consider the possibility of accidental death (trauma, poisoning, scalding, drowning)
- To consider the possibility of asphyxia/airway obstruction
- To consider the possibility of non-accidental injury
- To document the presence/absence of pathological processes and to contribute to the multidisciplinary clinicopathological evaluation of the death.

Clinical information relevant to the autopsy

The pathologist should have a comprehensive history and report on the circumstances of death, prior to starting the post-mortem examination. Ideally, available information should include:

- detailed history, including details of pregnancy, delivery, post-natal history, ante-mortem history and precise circumstances of death including family history (previous sibling deaths, consanguinity, drug use, sleeping arrangements)
- event-scene investigation report from paediatrician and/or police officers if available
- any police sudden death report or report of the coroner's officer
- GP records
- reference to the child protection register
- reference to resuscitation procedures
- results of examination by a consultant paediatrician
- results of septic screen, if done in an ED department
- details of any other investigations sent from the ED department, and any results available so far. All results from such investigations should be reviewed by the pathologist as well as by the Designated Doctor Child Deaths.

The autopsy procedure

- If there is any suspicion of abuse contributing to the death, inform the coroner immediately.
- Consider close adherence to the rules of evidence from the outset of involvement (e.g. identification and corroboration of evidence).
- Full autopsy (external and internal examination), with attention to: weights, measurements, presence/absence of secretions or blood around nose and mouth

and petechial haemorrhages on face, conjunctivae or oral mucosa (consider photography for documentation of dysmorphism and/or evidential purposes).

- Any evidence of injury (a full skeletal survey reported by a paediatric radiologist is mandatory in such cases).
- Weights of all major organs.
- If suspicious of intracranial injury, no needles should be placed within the skull or the eye until the scalp, skull and intracranial contents have been examined and injury excluded.

Specific significant organ systems

All organs to be systematically examined.

Organ retention

- If trauma to the brain/spinal cord is suspected, consider retaining these organs; also consider retaining the eye for specialist neuropathological referral.
- In general, if the clinical history and pathological findings require any particular organ to be retained for further assessment, this should be discussed with the coroner's office.
- If the clinical history and pathological findings require any particular organ to be retained for further examination this must be discussed with the coroner's office immediately. Confirmation of all tissues retained, whether fluids, tissue samples or whole organs, must be confirmed by fax to the coroner's office at the time of notifying the initial result of the post mortem examination.

Minimum blocks for histological examination

- Five lobes of lung (H&E, and Perls' method for iron)
- Heart (free wall of left and right ventricle, interventricular septum)
- Thymus
- Pancreas
- Liver
- Spleen
- Lymph node
- Adrenal glands
- Kidneys
- Costo-chondral junction of a rib to include bone marrow sample
- Muscle
- Blocks of any lesion, including fractured ribs
- Brain: 10 to 14 blocks including cerebral hemispheres, basal ganglia, hippocampi, thalami, brainstem, cerebellum, meninges and spinal cord; dura if there is haemorrhage
- Samples to be frozen at -80 °: kidney, heart, liver and skeletal muscle. Consider freezing heart if suspicion of a cardiovascular condition.

(In cases with no clinical evidence or macroscopic autopsy findings explaining death, it is strongly recommended that the brain is examined only after adequate fixation, for one to two weeks).

If any organ is to be retained for fixation and more extensive sampling, this must be discussed with the coroner and the appropriate authority obtained. This may necessitate a delay in the funeral arrangements to allow return of the organ(s) to the body after fixation and sampling.

Other samples required (if not already taken in the ED department)

- Bacteriology (blood, cerebrospinal fluid, upper respiratory tract, bronchial swab and lung swab, faeces and any infective lesion).
- Virology (nasopharyngeal swab, lung, cerebrospinal fluid and faeces if indicated).
- Consider agreeing protocols with local medical microbiology departments to use modern DNA amplification techniques for organism recognition.
- Biochemistry (urine, if present, for metabolic investigations and toxicology; blood and bile spots on Guthrie card for acylcarnitines by mass spectrometry if metabolic disease suspected or if fat stains on frozen sections are positive).
- Frozen section – stained with Oil Red O for fat on liver and kidney, skeletal and cardiac muscle (mandatory in all unexplained unexpected infant deaths).
- Toxicology (peripheral blood, whole unpreserved and in fluoride bottle, urine, bile, stomach content; request an illicit drug/alcohol screen, specify other drugs as indicated from the history). The chain of evidence should be preserved.
- Skin sample for fibroblast culture.
- Haematology: 2 ml blood in EDTA for normoblast count (if less than 3 days interval).

Clinicopathological summary and report to the coroner

- Summarise the clinical history and main pathological findings without quoting verbatim from any police report.
- Consider whether the pathology satisfactorily explains the clinical circumstances of the death.
- Consider whether there are features indicating a familial/genetic disease requiring screening.
- Consider whether there are features sufficient to suggest non-accidental injury or neglect.
- The coroner must be informed of the result of the initial post mortem examination as soon as practicable and certainly on the same day the examination took place. If a complete and sufficient natural explanation of the death is identifiable usually no inquest will be required.
- If, during the initial post mortem, findings emerge that clearly identify neglect or abuse as the most likely explanation for the death, the coroner must be immediately informed and the police will become the lead investigating agency. The provisions of normal criminal investigations will be set in motion, including the requirements of the Police and Criminal Evidence Act 1984.
- If, in the light of initial post-mortem findings (including careful consideration of the circumstances of the death), there is no clear or sufficient natural cause

of death – *whether or not there are some concerns about the possibility that abuse or neglect might have contributed* – the initial 'cause' of death should be given to the coroner as "unexplained pending further investigation". In these circumstances, the continued close cooperation of all agencies will be of great importance, and the nature and content of any further investigations by the police or social services department will be determined by the strategy discussion immediately after the initial post-mortem results are available.

- The use of the term "unascertained", which carries implications that the death may have been the result of neglect or abuse, should generally be avoided.
- The report must include details of any samples taken or kept and instructions for their further retention or disposal, as authorised by the coroner.
- A full report, including the results of all further investigations undertaken (e.g. histology, microbiology, toxicology, radiology, virology, histochemistry, biochemistry or metabolic screening of blood or other samples), should be prepared and made available to the coroner and to the multi-professional local case discussion meeting, usually held 8–12 weeks after the death and chaired by the Designated Doctor Child Deaths.
- The pathologist should, if possible, attend and take part in the multi-professional local case discussion meeting.

Child death proforma

Name of child:________________

Hospital Number:______________

Date:

Time:

History

Essential history to aid immediate resuscitation and

investigation (a very full history will be taken at home visit)

Person(s) accompanying child | Relationship to child

____________________________ ____________________________________

____________________________ ____________________________________

____________________________ ____________________________________

Presenting history

Record

- The immediate event
- Who found the child and when
- The circumstances in which the child was found.

Document history given by parent, police, ambulance, other and who is present for each part of history taking:-*Use extra sheets if necessary and remember to document who gave history on all sheets.

Past medical history

Record birth and perinatal history, admissions, OPD, A&E attendances.

Brief family history

Record names of parents/carers, addresses, ethnicity, health, parental mental health problems / social problems where possible. Record household composition, significant other adults and children in the household

FH of sudden deaths / deafness?

Name of child:________________

Hospital Number:______________

Systemic enquiry

CVS

(Including apnoeas, ALTEs)

RS

GIT

UT

CNS

Name of child:________________
Hospital Number:______________

Child death proforma

Use separate ED proforma to record resuscitation details

Examination

Examining Doctor
examination

Persons present during

Name (PRINT)
____

Designation:
____

1.
2.
3.
4.

Clothing

Note condition of clothing including staining with blood or vomit and site. Remove clothing with care and seek advice of police re: procedure for preserving evidence. Condition of nappy if used.

Weight: ______________kgs
_________________centile

Head circumference: ______________cms
_________________centile

Rectal temperature: ____________________

General examination

In addition to routine examination, be sure to look for and document signs of neglect, cleanliness, appearance of hair, nails and teeth, pallor, nappy rash, infestation, bloating, interaction from care-giver.

Eyes

Cloudy cornea / fundi / conjunctival haemorrhages

Ears

Presence of fluid / blood / injury

Left Right

Mouth

Frenulum / abnormalities of teeth / other abnormalities

Note any blood or other fluids

Nose

Presence of blood / other fluids / injuries

Name of child:________________ Hospital Number:______________

Presence of injury

Bruising	Yes	No	No

If present record on body chart and consider photography

Presence of livido (post mortem changes)	Yes	No

If present record on body chart

Document puncture sites from resuscitation

Genitalia and anus

Describe any obvious injuries or abnormalities

Record how the parents were supported

Investigations:

Note: investigations MAY be done DURING resuscitation as part of investigation of child's collapse

INDICATIONS FOR INVESTIGATIONS AFTER CHILD PRONOUNCED DEAD

NONE usually required

IF – WEEKEND OR BANK HOLIDAY – femoral vein for Blood Culture and Pink EDTA bottle for "normoblast" assay
If asthma / anaphylaxis death, consider tryptase

Complete Notification of Child Death form and fax (include police & their contact details

Police accompanying child:

Name ID number Mobile phone details

______________________ ___________ -
____

______________________ ___________

____

Reported cause of death	Autopsy N %	PMCT N %
Cardiac failure	12 43	8 42
Haemorrhage	7 25	6 32
Cardiorespiratory failure	2 7	1 5
Multi-organ failure	2 7	1 5
Acute respiratory failure	2 7	1 5
Lung emboli	1 4	1 5
Meningoencephalitis	1 4	0 0
None proven (intrauterine death)	1 4	1 5

Total-a	28	19
Diagnostic group		
Diseases of the circulatory system	22 54	18 69
Infectious and parasitic diseases	6 15	0 0
Diseases of the respiratory system	4 10	4 15
Diseases of the digestive system	2 5	1 4
Neoplasms	2 5	2 8
Diseases of the nervous system	2 5	1 4
Congenital malformations, deformations and chromosomal abnormalities	1 2	0 0
Injury, poisoning and certain other consequences of external causes	1 2	0 0
None proven (intrauterine death)	1 2	1 4
Total-b	41	26

a- One case excluded (no autopsy due to infection risk)

b- Sum exceeds number of patients because in some cases, several

Systems/pathologies were involved equally (Westphal et al., 2012)

7.6 Appendix III Libyan government funding letter

Libyan Embassy سفارة ليبيا

Cultural Attaché - London الملحقية الثقافية – لندن

وزارة التعليم العالي والبحث العلمي

Ministry of Higher Education & Scientific Research

University of Sheffield
Western Bank
Sheffield
S10 2TN
United Kingdom

Ref: IK144-538-49581
Date: 23/03/2017

ENROLMENT CERTIFICATE - CONFIRMATION OF SPONSORSHIP

Student Name:	Mr Mohamed Mohamed Ben Taher	**Student No:**	9414
Course Name:	HMC CLINICAL FT	**Your Ref:**	
Starting Date:	08/03/2017	**Tuition Fees:**	£0.00
Academic Year:	2016/2017	**Bench Fees**	£2,000.00
Study Year:	3/3		
Degree:	PhD	**Total Fees:**	£2,000.00

Dear Sir/Madam,

We hereby confirm that the above named is a Libyan Sponsored student and the Cultural Affairs Dept. At the Libyan Embassy in London is responsible for his/her tuition fees for the academic year stated above and subject to the Terms & Conditions provided overleaf.

Please note that non-compliance with our Terms & Conditions relieves us of the responsibility to pay invoices sent to our office.

Thank you in advance for your time and co-operation and do not hesitate to contact us if you require further information.

Yours Sincerely,

23/3/2017

Dr. Abdelbasit Gadour
Cultural Attaché

Cultural Attaché
Libyan Embassy - UK

7.7 Appendix IV BJR journal permission

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7.8 Appendix V ethical approval of questionnaire study

The University Of Sheffield.

Downloaded: 08/01/2016
Approved: 08/01/2016

Mohamed Ben Taher
Registration number: 140134302
Human Metabolism
Programme: PhD Medicine

Dear Mohamed

PROJECT TITLE: Public Perception of using Medical Imaging to Identify Causes of Death in Children amongst the Libyan Communities In Libya and Sheffield.
APPLICATION: Reference Number 007234

On behalf of the University ethics reviewers who reviewed your project, I am pleased to inform you that on 08/01/2016 the above-named project was **approved** on ethics grounds, on the basis that you will adhere to the following documentation that you submitted for ethics review:

- University research ethics application form 007234 (dated 21/12/2015).
- Participant information sheet 1014367 version 1 (15/12/2015).
- Participant information sheet 1014368 version 1 (15/12/2015).

The following optional amendments were suggested:

see comments above

If during the course of the project you need to deviate significantly from the above-approved documentation please inform me since written approval will be required.

Yours sincerely

Jean Lazenby
Ethics Administrator
Medical School