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Optimising Radiation Dose of CT Pulmonary Angiogram for Imaging Pulmonary Embolism and Alternative Acute Respiratory Diseases

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Statement of Authorship

I, Ahmed Hashi, hereby declare that this thesis submission is my work and that it contains no material previously published or written by another person except where acknowledged within the text. This thesis does not contain any material that has been accepted for the award of another degree or diploma in any university.

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Abstract

CT pulmonary angiogram (CTPA) is utilised to diagnose pulmonary embolus in various clinical settings. CT imaging has considerable advantages over other imaging modalities. Whilst considering its widespread application and advantages, it tends to have high radiation exposure. Additionally, there are high rates of suboptimal and non-diagnostic examinations that result in unnecessary radiation dose. Therefore appropriate radiation dose reduction techniques are required without compromising imaging quality; unfortunately, efforts to reduce radiation dose can also diminish image quality and lead to missed pulmonary emboli and other lung pathologies.

Several studies have investigated 80kV CTPA protocols and found a considerable upsurge in image noise and reduced imaging quality. The purpose of this research project was to develop an 80kV CTPA protocol with reduced imaging noise, decreased radiation dose and simultaneously reducing suboptimal examinations in patients with suspected pulmonary embolism. Both qualitative and quantitative approaches were conducted to achieve this purpose.

This study has demonstrated that the new 80kV CTPA protocol can significantly ($t(60) = -17.8$, $p < 0.05$) reduce patient mean effective radiation dose by 66% with a mean radiation dose 1.005mSv compared to 3.03mSv with current 100kV protocols. The study has also demonstrated a reduced rate of suboptimal examinations and a significant increase ($t(75) = 9.1$, $p<0.05$) in contrast enhancement of the pulmonary arterial tree at the 80kV exposures. It has also been found that a gentle breath-hold open mouth technique with an 80kV scanning protocol also improves imaging quality.

In terms of imaging quality assessment, the improved 80kV CTPA yielded acceptable image quality comparable to the standard protocol as per the radiologist assessment.

This study's original contribution to knowledge is introducing a new, improved 80kV CTPA that allows the imaging departments to achieve an excellent contrast enhancement and lower suboptimal examinations. This study's overall significance is a demonstrable reduction in radiation dose without affecting the CTPA image quality in the majority of the patients.

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List of Abbreviations

ABG	Arterial Blood Gas Analysis
AIDR 3D	Adaptive Iterative Dose Radiation
CAD	Coronary Arterial Disease
COVID-19	Coronavirus Disease of 2019
CTDI	Calculated Tomography Dose Index
CTPA	CT Pulmonary Angiogram
DLP	Dose Length Product
DVT	Deep Venous Thrombosis
ECG	Electrocardiogram
ESR	Erythrocytes Sedimentation Rate
FIRST	Forward-Project Model-Centred Iterative Reconstruction Solution
G	Grey
IQR	Interquartile Range
MRA	Magnetic Resonance Angiography
MRI	Magnetic Resonance Imaging
mSv	MilliSievert
PACS	Picture Archiving and Communication System
PCI	Percutaneous Coronary Intervention
PE	Pulmonary Embolism
PERC	Pulmonary Embolism Rule-Out Criteria
PIOPED II	Potential Examination of Pulmonary Embolism Diagnosis II
SD	Standard Deviation
SPN	Solitary Pulmonary Nodule
US	Ultrasound

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Chapter 1: Background Information on Pulmonary Embolism

1.1: Section One: Introduction

Pulmonary embolism (PE) is a severe cardiovascular illness recognised as a significant contributor to morbidity and mortality among the community and hospitalised patients[1]. PE is the third most common cardiovascular diagnosis following myocardial infarction and stroke [2]. Most pulmonary emboli emerge due to blood clots in the legs called deep vein thrombosis (DVT). Thrombus or blood clots can form in any vein due to stasis of blood, vascular injury and hypercoagulability. The thrombus may then embolise or travel to more proximal veins, eventually lodging in the pulmonary arterial system. A massive acute embolus can lodge in the large pulmonary arteries, cause sudden loss of right ventricular output, and lead to death. Even smaller emboli, can cause respiratory symptoms, chronic PE can lead to marked lung function reduction and pulmonary hypertension, which are significant causes of morbidity and can contribute to mortality[3]. Hence timely diagnosis and treatment are required to prevent death and both medium and long term morbidity

CT pulmonary angiogram (CTPA) is the preferred imaging test for diagnosing pulmonary embolism. While formal pulmonary angiography is considered the gold standard, it is almost never utilised as it is invasive and carries much higher radiation and contrast risks. CT imaging, in most cases, has considerable advantages over other types of imaging modalities; these include widespread availability (day and night), fast imaging acquisition, fast turnaround times, high diagnostic accuracy and low risk with regards to contrast reaction. For clinicians, CTPA also diagnoses alternative diseases where pulmonary embolism is not the symptoms' source. CTPA is also easier to interpret for physicians. These considerable advantages have led to the overuse of CTPA in this imaging department. Multiple factors contribute to increased CTPA utilisation[4]. Among the multitude of factors, the most common are non-specific symptoms of PE, emergency department overcrowding and physicians' fear of failing to obtain a diagnosis, as discussed in the following paragraphs.

One of the most significant factors leading to the increased CTPA requests is that pulmonary embolism symptoms are often non-specific. Patients may experience similar symptoms in acute respiratory or cardiac diseases; 18% of patients who had CTPA for the possible PE were found to have other conditions requiring treatment such as pneumonia, pulmonary oedema, malignancy, large pleural or pericardial effusion[5, 6].

Validated risk assessment tools such as Wells, PERC and Geneva scores approximate probability rather than give definite answers; this is often inadequate for management decisions. The validation of these tools may also not be accurate in the current patient cohort, especially in the

emergency department (ED) setting, and these tools are highly dependent on clinician experience. Thus the diagnosis of pulmonary embolism remains a challenge.

Overcrowding in emergency departments is also another factor influencing the higher CTPA requests. According to a report released by the Australian Institute of Health and Welfare, approximately eight million ED presentations occurred in Australia within the financial year 2017-2018 [7]. The Australian Capital Territory (ACT) handled 147,778 ED presentations and also had the longest median waiting time in Australia, only 28% of urgent patients were attended in the accepted timeframe, and ACT EDs are often at or near full capacity and sometimes above[7, 8].

Other organisational factors contributing to increased CTPA requests include inadequate numbers of trained physicians, reduced hospital beds availability, ED funding being contingent on time to diagnosis or discharge and hospital financial constraints. These factors combine to hasten diagnosis and management. Current ED planning, called the 'fast-track approach' aims to save on costs, increase patient satisfaction, enhance patients' flow, and decrease the average waiting time. Conversely, the 'fast-track approach' has led to physicians' reduced time to ask a proper history, perform a precise examination, and have de-emphasised basics testing. For instance, electrocardiography (ECG), D-dimer, arterial blood gas (ABG) examination, and chest radiography have also reduced the ability to utilise validated risk assessment tools. Data analysis performed in the hospital record system revealed that over 50% of patients underwent CTPA in the absence of the D dimer test. This occurred even though most doctors (referred to as 'medical doctors' from herein) recognised that D-dimer testing is essential in helping identify patients with low risk to prevent unnecessary radiation exposure to radiation in low-risk patients.

Another aspect that affects CTPA requests is the fear of missing the diagnosis. This can be fatal due to massive PE circulatory collapse; this is considered negligence in most cases. Medical doctors view CTPA as an essential tool to decrease the possibility of missing the diagnosis. Therefore inexperienced physicians may over utilise CT, this being called 'defensive medicine'. According to the American College of Radiology's clinical decision support systems assessment, only 27% of CT scans in younger patients were appropriate[9]. CTPA may be used as a screening tool, the number of positive PE in this imaging department is lower (11%) than that reposted in the current literature, which was 12.0% to 28.1%[10]; a higher a positive PE rate of 17.8% and 15% in emergency departments in Canada[11, 12].

Although many health providers practice defensive medicine, this always leads to a waste of valuable resources, an upsurge of radiation exposure with clear benefits to the patient. It also sharply escalates the price of medical treatment.

Radiation exposure is a significant concern as a CT scan is the largest contributor to medical radiation exposure, accounting for nearly half of the combined effective dose of all other imaging modalities combined[13]. The standard CTPA examination is a high exposure procedure with the current standard protocols mean effective dose was 5.9mSv at 120kV or 3.03mSv at 100kV as seen on inspections at this facility. CT pulmonary angiogram was also reported to have an even higher mean effective dose of 4.5 mSv across 34 CT scanners surveyed in Ireland[14].

Moreover, it is recognised that radiation exposure is linked to the possibility of suffering from cancer, radiation-induced cancer risk-sensitive organs include ovary, salivary gland, female breast, oesophagus, liver, lung, prostate, urinary bladder, brain and thyroid[15],[16]. The high radiation exposure also triggers fears amongst patients concerning radiation exposure. Therefore clinicians need to utilise the lowest possible radiation dose, particularly for young and pregnant patients, since these high doses may cause greater harm.

There are various dose reduction methods available, such as reducing the anatomical scan coverage and tube peak kilovoltage (kV) to 80kV and utilising less tube current (mAs), using Iterative reconstruction algorithms, and a higher helical pitch. A high helical pitch and decreased anatomical coverage may reduce radiation exposure to some extent, but reducing either the tube voltage or mAs may offer substantially more radiation dose saving.

Tube current (mAs) reduction can be used to decrease the radiation dose. There are significant radiation dose savings in decreasing the tube current, and utilising a tube voltage of 120kV and fixed reduced tube current of 66mAs may generate imaging quality outcomes comparable to 110mAs [17]. However, there are two problems with using fixed- low mAs. Firstly using low tube current decreases CNR compared with a normal radiation dose protocol [18]. Secondly, there was noticeable image quality degradation, mainly increased image noise and streak artifacts[19]. It is hard to offer an accurate exposure for variable patient sizes with fixed mAs except when a technique chart is utilised, which is impractical in a busy imaging department. Therefore an alternative method is to decrease tube voltage (kV) while using tube current (mAs) modulation that adjusts tube current to identify the patient anatomy/thickness [20-24]. Tube current modulation reduces the radiation exposure in lower attenuation sections of the anatomy to offer adequate image quality whilst decreasing the radiation dose.

Tube voltage reduction to 80kV may offer a considerable reduction in radiation dose. 80kV protocol offered an acceptable image quality with decreased radiation dose amongst patients weighing less than 75kg; nevertheless, in patients weighing more than 75kg, image noise increased markedly with weight [23].

Several studies have examined the utilisation of lower tube voltage of 80kV and found a significant reduction in radiation dose, but with a considerable upsurge in image noise which reduced

diagnostic confidence in detecting pulmonary embolism[18, 24,25-27.] Therefore, imaging departments in Australia utilise a 100kV or 120kV CTPA protocol that has a high radiation dose because of image noise with lower kV protocols.

Therefore, new research is needed to examine approaches to reduce radiation dose and image noise without affecting diagnostic quality.

Another major limitation observed with the current CTPA protocols is the high number of suboptimal or non-diagnostic examinations because of low-contrast enhancement or motion artefact[28]. Many of these patients may require repeat examinations or VQ scans; thus, this radiation exposure was unnecessary[28]. Different factors may result in suboptimal examinations such as restricted venous access, low or sluggish contrast flow to peripheral pulmonary arteries, an incorrectly placed region of interest (ROI) triggering the scan, Valsalva from improper breathing technique, insufficient cannulation flow rate, beam hardening artefact from contrast column in the IVC and respiratory motion artefact[29].

Another issue that causes more suboptimal examinations in pregnant patients is that physiological tachycardia leads to ventricular contrast filling with each cardiac cycle resulting in lower contrast pulmonary truck opacification. Hence in pregnant patients, it becomes difficult to achieve steady contrast opacification with the pulmonary trunk. This issue causes recurrent non-diagnostic studies with pregnant patients ranging from 12% to 35.7%, as reported in several studies.[28, 30]. A study in Memorial University hospital in Canada by Hogan et al. (2019) with pregnant and postpartum women showed an even higher rate of suboptimal examinations with 43% due to mainly low contrast enhancement or Valsalva.

Suboptimal examinations also occur more commonly among overweight patients undergoing a 120kV protocol CTPA. There are no studies specifically examining the image quality of larger patients. However, a retrospective study of 3612 CT pulmonary angiogram examination revealed a 6% rate of indeterminate studies, and body habitus was listed as the main reason for the poor image quality[30]

The two issues that are believed to cause higher rates of suboptimal examinations in a larger patient are the exaggerated Valsalva phenomenon and reduced contrast opacification because of higher kV. The exaggerated Valsalva is seen because larger patients tend to take in larger breaths and therefore cause a greater degree of reduced cardiac output with inspiration and increased cardiac output with expiration, the end results in diluted contrast in the pulmonary arteries.

The research gap is how to reduce the increased image noise whilst reducing CTPA dose and, therefore, maintaining diagnostic confidence in detecting pulmonary embolism. New research needs to examine how to simultaneously decrease the radiation dose, image noise, as well as suboptimal

examinations. Hence, we proposed a study to examine alternative ways to reduce radiation dose, the suboptimal examination of CTPA without impacting the image quality.

1.1.1: Research Aim

The primary aim of this research is to reduce radiation exposure of CT pulmonary angiogram (CTPA) examinations without compromising the image quality in patients weighing less than 105kg.

This study adheres to a limit of 80kV in patients weighing less than 105kg because a small trial of patients found that patients weighing more than 105kg required higher tube voltage (100kV); this is further discussed in chapter 6, section four.

1.1.2: Research Question

How can imaging departments reduce radiation dose and maintain diagnostic confidence in detecting pulmonary embolism using the novel 80kV CTPA protocol (also referred to as 'improved 80kV CTPA' from herein) compared to the standard 100kV CTPA protocol in patients weighing less than 105kg?

1.1.3: Objectives

The best methods to decrease radiation in patients with suspected pulmonary embolism are reducing radiation dose, reducing suboptimal or non-diagnostic exams, and decreasing the number of unnecessary CTPA referrals. Hence the objectives of this study are:

1. To determine factors that contribute to CTPA overuse and explore ways to reduce over-ordering CT pulmonary angiogram.
2. Create a low dose CTPA protocol with 80kV low image noise while using adjusted tube current standard deviation and improved image reconstruction processing.
3. To determine whether the confidence in detecting pulmonary embolism with the improved 80kV CTPA protocol is acceptable to clinicians compared to the standard 100kV protocol?
4. To determine whether the improved 80kV CTPA protocol with gentle breath-hold with open mouth technique is effective for decreasing suboptimal CTPA examination in patients weighing below 105kg?

1.1.4: Thesis Hypothesis

H0:1) The mean radiation dose of the improved 80kV CTPA is lower than the mean radiation exposure of the 100kV protocol and still provides diagnostic confidence equal to that of the 100kV standard protocol.

H0:1.1) Improved 80kV CTPA with gentle breath-hold and open mouth allows excellent contrast enhancement of the pulmonary arteries and a lower percentage of suboptimal examinations, yet a considerable decrease in patient radiation dose without affecting the image quality.

1.1.5: Study Scope

This thesis hopes to enhance imaging for patients with suspected PE in three ways:

1. This study will examine the actual cause of CTPA over-utilisation and then aims to recommend ways to reduce the increasing number of CTPA. Chapter four of this thesis explores the leading cause of CTPA over-utilisation by utilising a retrospective observational study of CT scanning data from a single large tertiary hospital imaging facility and a survey of medical doctors in the same facility. This chapter shows valuable information about the cause of CTPA over-ordering, the percentage of pulmonary embolism actually found on these scans, the number of suboptimal studies and the mean effective dose utilising the standard CTPA protocol. This chapter revealed that accurate differentiation with better history, clinical examination and basic examinations (ECG, chest radiograph, D-dimer, biochemistry) as well validation tools such as probability testing greatly reduced the need to perform as many CTPA examinations.
2. This study aims to formulate a low dose pulmonary angiogram protocol that will decrease the radiation dose to its lowest adequate quantity whilst retaining diagnostic sensitivity in PE suspected patients weighing below 105kg. Chapter five discusses the improved CTPA protocol, image quality assessment and radiation dose compared to the standard 100kV CTPA.
3. This study aims to reduce suboptimal exams. Chapter six discusses the method of gentle breath-hold with an open mouth whilst using the improved CTPA protocol and high injection rate 5ml/sec in an effort to reduce Valsalva and improve contrast enhancement within the pulmonary arteries. The combination of these methods decreased suboptimal imaging quality and improved contrast enhancement amongst patients undergoing CTPA; most patients tolerated the breathing method.

1.1.6: The Design of the Study

This study was performed after the Hospital Research Committee's approval (ID: 15-2017) and the Australian National University (ID: 2020/386). In order to fulfil the objective of this study, the research method chosen to collect data was a combination of both qualitative and quantitative techniques.

1.1.7: The Value of the Research

The primary value of the study is to decrease the exposure of radiation to patients. This will help patients to receive less radiation than the standard dose, which will, in turn, decrease the probability of suffering from radiation-induced cancer during their lifetimes. Another value of the research is that it will improve pulmonary arterial tree enhancement and reduce suboptimal images which are a significant problem in most imaging departments; suboptimal imaging cause increased patient radiation dose with repeat examinations and increased diagnostic uncertainty.

1.1.8: Involvement in the Research

Before performing this research, I competed for a Masters of Medical Radiation Science and radiographic image interpretation specialisation at Sydney University, which gave me enhanced knowledge and skills in radiology image interpretation and a good foundation for optimising CT radiation dose. Since then, I have participated extensively in audits of radiation doses in several medical imaging departments to ensure that CT examinations that were conducted were within the accepted Australian national diagnostic reference level service (NDRLS). The NDRLS provide radiation dose data from other imaging facilities that this facility data is benchmarked against; they provide indicative levels which should not be exceeded under normal conditions. Radiation dose audits provided me with reinforcement to further research approaches to decrease radiation dose without compromising image quality.

During my time in medical imaging, I have also seen the growth rate of CTPA referrals submitted for either pregnant or young patients, which has caused patients anxiety. This influenced me to conduct this study. Furthermore, ACT health senior radiologists were concerned about the growing rate of CTPA referrals and encouraged me to undertake this research project.

1.1.9: Structure of the Thesis

Chapter one and introduction provides background information to introduce the reader to the research, its purpose, the study's aim, and its inception. This chapter outlines PE imaging issues such as radiation exposure, CT overuse, low-contrast enhancement, non-diagnostic examinations and

stipulates the study objectives. Additionally, it discusses the field of anatomy that is scanned, the chest pathologies and systematic methods in interpreting chest imaging.

It also outlines the similarities of the signs and symptoms between acute respiratory differential diagnosis and pulmonary embolism, which was essential in understanding the issue of overuse. Understanding the overlap between the ailments is vital in developing a protocol that would diagnose pulmonary embolism and other acute respiratory illnesses.

Chapter two presents a relevant literature review of the research project; tube current, tube voltage pitch, dual CT scanners and cause of image noise were outlined in this chapter.

Chapter three deliberates on the development and methodology of the novel improved 80kV CTPA. It discusses the methods through which the study was performed, such as the use of both quantitative and qualitative methods, including questionnaires and case studies. This chapter also demonstrates that the methods were suitable, attainable and directed towards helping to reduce radiation exposure.

Chapter four presents the retrospective review involved reviewing patient records to gather data to better understand the problem of CTPA over-utilisation and reasons for over-ordering. This study evaluated CTPA examination conducted at a tertiary facility to identify the number of PEs, additional diagnoses on CTPA, rate of suboptimal imaging and dose from standard dose CTPA. It also presents the findings obtained from questionnaires administered to medical doctors regarding the differential diagnosis of pulmonary embolism; this confirmed the observational study results.

Chapter five outlines the finding of a case-based comparative study of the improved 80kV CTPA protocol versus the standard CTPA protocol. The primary objective was to evaluate the radiation dose and image quality of the improved 80kV CTPA versus the standard 100kV protocol. The research showed that the low-dose protocol decreased radiation without reducing image quality or diagnostic accuracy.

Chapter six discusses the findings of a case-based comparative study on approaches to decrease suboptimal examinations; this utilised new breathing methods and education with the improved 80kV CTPA protocol. This study aimed to reduce the rate of suboptimal CTPA examinations using a gentle breath-hold open mouth technique with low tube voltage (80kV), patient education, and a high injection rate acquisition technique. The research showed a reduced rate of suboptimal CTPA.

Chapter seven concludes these with a discussion and conclusion linking the finding with the research objectives and hypotheses. It additionally presented limitations and recommendations on future improvements to CTPA protocols.

1.2: Section Two: Lung and Heart Anatomy and Physiology

This section initially discusses anatomy, including lung, heart, veins and arteries and the physiology by which the deoxygenated and oxygen blood moves to and from the heart and lungs. The chapter also discusses enhanced approaches to assessing chest x-rays as it is adequate to diagnose most acute respiratory diseases.

1.2.1: Lung Anatomy

Lungs are respiratory organs where the exchange of gases takes place. Lungs offer an alveolar surface area of approximately 40 m^2 in which gaseous exchange takes place [31]. Lungs occupy the majority of the thorax and are protected by the ribs. The lungs are bounded by the ribs on nearly all sides excepted inferiorly, where there is the diaphragm. To allow movement with breathing, the thoracic cavity is lined by a pleura that glides the surrounding structures' lung surfaces.

Each of the lungs can be separated into lobes, as in figure 1.1. The right lung has three lobes: the upper, middle, and lower lobes; the left lung is divided into upper and lower lobes[32]. The divisions between lobes are called a fissure, and both lungs have an oblique fissure that divides the upper and lower lobes, the right lung as an additional horizontal fissure that divides the middle lobe from the right upper lobe[33, 34].

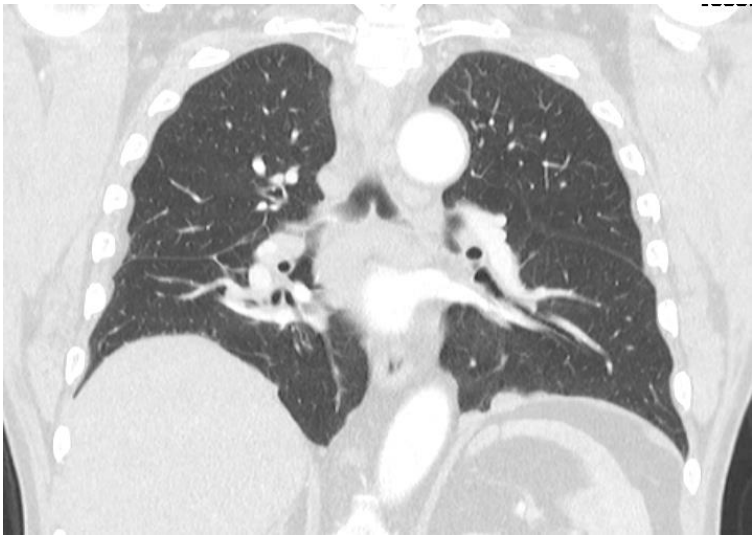


Figure 1. 1. Low dose CTPA illustrating lung anatomy.

In the above oblique and the horizontal fissures are shown above, the right lung has three lobes, and the left lung has only two lobes divided by oblique fissures.

1.2.2: The Trachea and Bronchi

The trachea starts in the neck at C6, at the level of the cricoid cartilage. It ends at an angle of Louis T4/5, where the trachea divides into the right and left main bronchi. The bifurcation area is called carina, which is a vital landmark, particularly while utilising the bolus tracking within the CTPA.

Furthermore, the right main bronchus is broader, shorter, and more vertically oriented than the left main bronchus. The inhaled foreign bodies affect more in the right lobe due to vertically oriented position [35]. The main or primary bronchus at the hilum enters the lungs and then separates into the secondary bronchi. The secondary bronchi are connected to the lung lobes, in which they undergo further divisions. Each sub-division of the secondary bronchi corresponds to segments of the lobes, presented in table 1.1. Thereafter the bronchial tree divides progressively into smaller airways over several generations until it reaches the terminal bronchioles at the alveoli, where gaseous exchange occurs between the capillary blood and the alveolus[20]. While evaluating the CTPA, it becomes important to know the lung bronchopulmonary segment since arteries branches along with it.

Table 1. 1: Bronchopulmonary segments of the lungs.

Left Lung	Right Lung
Superior lobe ➢ Anterior segment ➢ Posterior segment ➢ Apical segment Middle lobe ➢ Lateral segment ➢ Medial segment Inferior lobe segments ➢ Superior ➢ Medial basal ➢ Anterior basal ➢ Lateral basal ➢ Posterior basal	Superior lobe ➢ Inferior lingular segment ➢ Apical segment ➢ Posterior segment ➢ Anterior segment ➢ Superior lingular segment Inferior lobe segments ➢ Posterior basal segment ➢ Lateral basal segment ➢ Medial basal segment ➢ Anterior basal segment ➢ Medial basal segment ➢ Superior segment

1.2.3: Is it a Pulmonary Artery or Vein?

While assessing the CTPA, it is essential to distinguish between the pulmonary veins and arteries because an unenhanced vein may look like PE.

1.2.4: Pulmonary Arteries

The pulmonary arterial systems transport deoxygenated blood from the right heart to the alveoli. The pulmonary trunk is the major artery; this divides into right and left main pulmonary arteries. The main pulmonary arteries divide into the lobar arteries, segmental arteries, and subsegmental arteries

until several generations of divisions supply the alveoli. The pulmonary artery on the left is smaller and shorter compared to the right. Every pulmonary artery inclines posterolateral to the primary bronchus before dividing into lobar and then segmental arteries[36]. The pulmonary arteries have a similar division organisation as the bronchial system, as noted in table 1.1.

When assessing CTPA, it is important to assess using a systematic and routine approach. Contrast enhancement allows assessment of at least the segmental arteries[20]. The branching pulmonary arterial system is visually demonstrated on CTPA on coronal reformats in figure 1.2. The pressure distribution within the pulmonary arterial system causes pulmonary embolism to occur more commonly occur in the lower lobes.

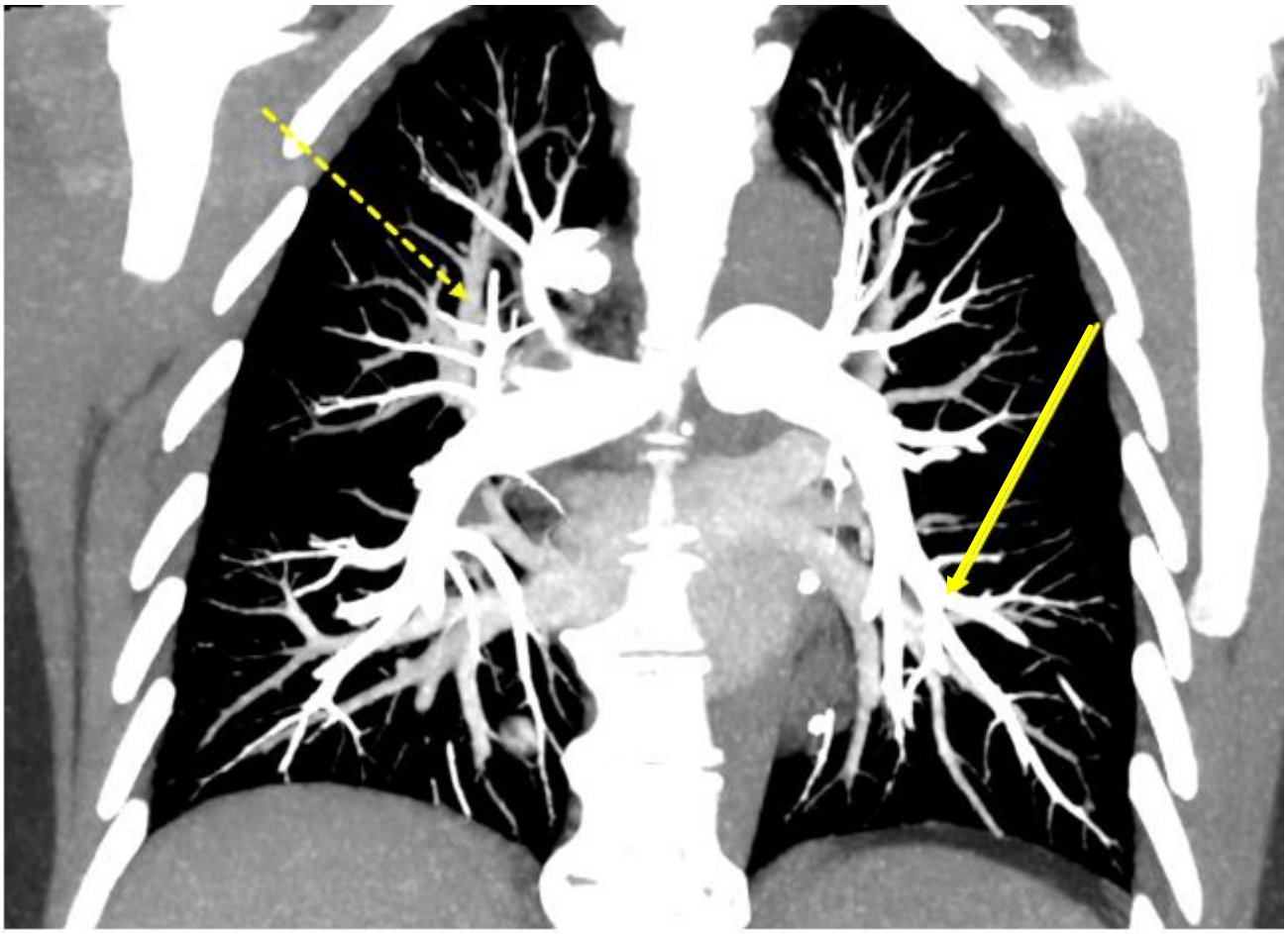


Figure 1. 2: Low dose MIPS CTPA with an accurate scanning range at a radiation dose of 1.02mSv. Solid arrow pulmonary artery, dashed arrow pulmonary vein.

The above improved 80kV CTPA shows clear visualisation of the segmental artery; it can easily be assessed while following the systematic routine approach. There is excellent timing contrast in the arteries, and there is less contrast on veins which indicate good timing, as shown by the dashed arrow.

1.2.5: Pulmonary Veins

Pulmonary venous systems drain oxygenated blood from the alveoli to the left atrium. The tributaries for the pulmonary venous system are organised along similar lines as the bronchi and the pulmonary arteries; they are organised from the alveoli into progressively larger veins until subsegmental and segmental veins, which supply the lobar and eventually the superior and inferiorly veins[37]. The pulmonary veins have a more horizontal approach before draining into the left atrium.

When performing a CTPA, it is vital to time the CTPA correctly and review the bronchopulmonary lung segments since arteries drain differently from the pulmonary arteries.

Figure 1.3 visually demonstrates blood flow in and out of the heart.

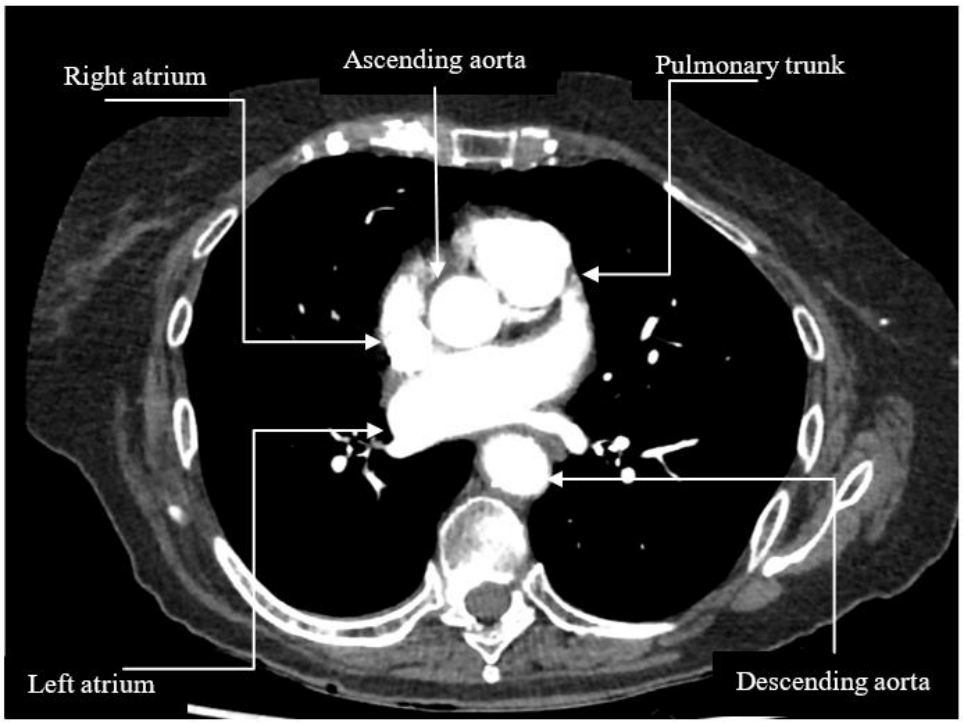


Figure 1. 3: Oxygenated blood brought back to the heart by the pulmonary veins in a low dose CTPA study.

1.2.6: Heart

The heart is a circulatory organ that pumps blood to the lung and to the body. The heart is a muscular organ. Heart muscles are composed of three distinct layers, which include the endocardium, myocardium, and epicardium. Endocardium may be described as a very thin endothelial layer that lines the heart's internal surface, including its valves. It also stretches and lines the blood vessels' internal lining. The myocardium takes the form of a thick layer that consists of strong cardiac muscles. On the other hand, Epicardium takes the form of a thin external layer in contact with the pericardium, a stronger layer covering the heart.

1.2.7: Chambers of the Heart

The heart has four chambers arranged in pairs, one each for the pulmonary and the systemic circulatory systems. The right heart supplies the pulmonary circulation, and the systemic circulatory system is supplied by the left heart. Each ventricle is paired with an atrium which receives the blood from the veins and forwards it onto the ventricles that pump the blood.

The interventricular septum further separates the inferior pumping chambers known as the ventricles. The right atrium gathers deoxygenated blood via the superior and inferior vena cava, cardiac veins and coronary sinuses (the hearts own vein) and sends them into the right ventricle. The right ventricle receives deoxygenated blood through the right atrium via the tricuspid valve and propels it through the pulmonary trunk to the lungs [31]. The interatrial septum further separates the right and left atria. The anatomy is illustrated in figure 1.4

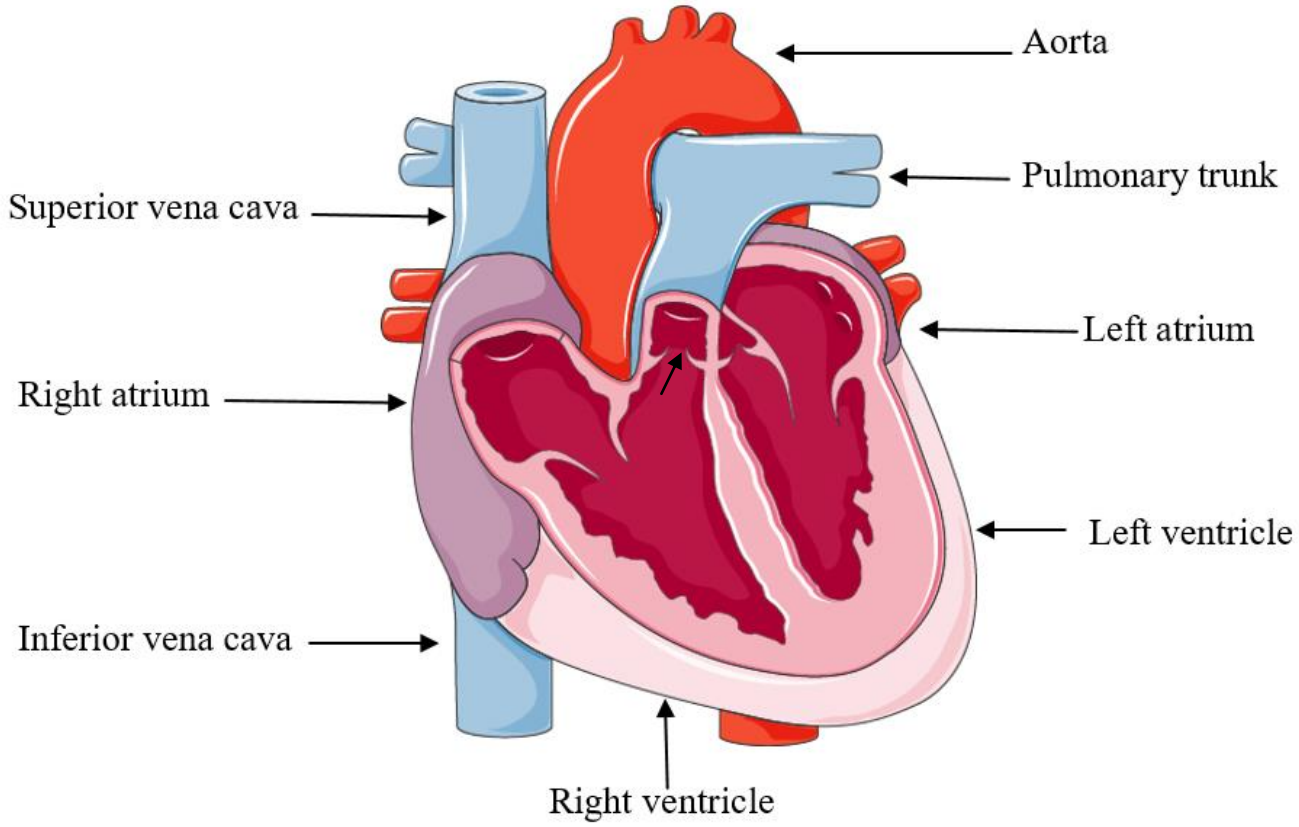
The thickness of the walls of the cardiac chambers depends on the function and required pressure required to pump in the circulation[31]. The atrial walls are thinner, and the left-sided chamber walls are thicker than the walls of the right-sided chamber because there is more pressure on the left side compared to the right side. Additionally, small muscles are present in the ventricle called papillary muscles that arise from the ventricles' inferior recesses; this anchors the valves cup and ensures integrity.

On a PA chest radiograph, the left ventricle comprises the majority of the left heart border and apex. A small left heart border near the hilum is formed by the left atrium and auricles (an anatomical side lobe of the atrium). The right heart border is formed by the right atrium and superior vena cava. On a lateral chest radiograph, the left atrium forms the heart's posterior wall with some contribution from the right atrium. Similarly, on a lateral chest radiograph, the heart's inferior heart border is formed by the left atrium but the right ventricle and pulmonary trunk from the anterior heart border. This is illustrated in figures 1.6 and 1.7.

1.2.8: CTPA Timing and Blood Circulation Through the Heart

The inferior and superior vena cava carries deoxygenated blood to the right atrium. The inferior vena cava drains blood from the lower body parts, whilst the superior vena cava drains it from the upper body parts. Nevertheless, both drain into the right atrium. The atrial blood is forwarded via the tricuspid valve into the right ventricle and via the pulmonary valve into the pulmonary trunk and circulatory system. During a CTPA, the goal is for scanning to begin when the right ventricle's blood containing contrast is pumped in the pulmonary trunk to ensure complete opacification of the pulmonary arteries with at least 180HU of contrast density in the pulmonary trunk.

The blood mixed with contrast then becomes oxygenated and is pushed back towards the heart via the pulmonary veins. This ultimately enters the left atrium and moves via the left ventricle's mitral valve and aortic valve into the aorta and systemic circulation. For CTPA, it is important to begin the scanning prior to contrast opacification of the pulmonary veins to ensure differentiation between pulmonary veins and pulmonary arteries. The speed with which the contrast reaches the pulmonary arteries depends on the cardiac output, cannula size and the contrast injection flow rate. For example, for patients with underlying heart conditions, contrast takes longer to reach the pulmonary trunk. Therefore a minimum of seven seconds is required to accommodate decreased cardiac output. With tachycardic or fast heart rate patients (including pregnant patients), the contrast may arrive at the pulmonary truck with three seconds. Hence a shorter delay time is required in this group.



Source: https://smart.servier.com/smart_image/heart-4/, creative commons licence[38]

Figure 1. 4: Right ventricle forces the blood through the pulmonary semilunar valve to the pulmonary arteries(arrowhead).

1.2.9: Lungs Lymphatic Drainage

The lymphatic network is a system of circulation throughout the body that drain leftover fluid from the systemic or pulmonary circulations back in the bloodstream via lymph nodes. The main role of lymphatic includes managing fluid levels in the body but is also important for infection control and

management of disease[31]. The intrapulmonary lymphatics drain into each hilar lymph node before being passed onto the mediastinal lymph nodes, the thoracic duct and eventually the subclavian vein.

It is significant to note that the lymphatic drainage blockage may result in the pleural effusion containing fat called a chylothorax.

1.2.10: Lungs Nerve Supply

The nerve serves as a significant breathing control component since they receive and pass motor information to the heart, diaphragm, and lungs. The phrenic nerve from the 3rd, 4th and 5th cervical roots run through the neck and mediastinum, eventually supplying the diaphragm's sensation. Intercostal nerves arise from the thoracic nerve root; they provide pain sensation to pleura and chest tissue: Vagus and the sympathetic nervous system supply pain sensation to bronchial, smooth muscle and mucous gland.

Furthermore, the pulmonary plexuses are located within each lung’s root and comprise the sympathetic fibres derived from the vagus pass. Its primary role is receiving motor information in and from the lungs[20]

1.3: Section Three: Chest X-Ray Evaluation

1.3.1: Assessment of Chest X-Ray

The evaluation of suspected PE patients involves a thorough history and physical examination, assessment of pretest probability, possibly arterial blood gas, pulse oximetry, D-dimer test, and chest x-ray. A chest x-ray cannot exclude a pulmonary embolism. It is a useful test for eliminating other acute respiratory issues, including pneumonia, pneumothorax, lung cancer, pulmonary oedema, pleural effusion, and atelectasis. A chest x-ray typically involves very small radiation exposure, and it is available in the emergency department. A chest x-ray is still the most commonly used imaging modality worldwide; however, interpretation can be difficult, and this is being less taught today even though it is a high demand skill required of doctors working in emergency setting[39].

The following section discusses a structured approach to chest x-ray image interpretation, which may help doctors enhance image interpretation skills and reduce CTPA overuse in patients with normal or visible pathologies.

1.3.2: Image Quality Evaluation

It is essential to evaluate the chest x-ray image quality by assessing various factors. First, the rotation is examined by evaluating the clavicle's medial position to ensure equal distance from the middle of the thoracic spinous procedure. Second, it is vital to ensure that patients get adequate inspiration; seven anterior ribs and costophrenic angles need to be seen for effective inspiration [40, 41]. Third, a chest x-ray with adequate exposure is best assessed by visualising the thoracic spine vertebrate and intervertebral disks through the heart in the lower thoracic spine.

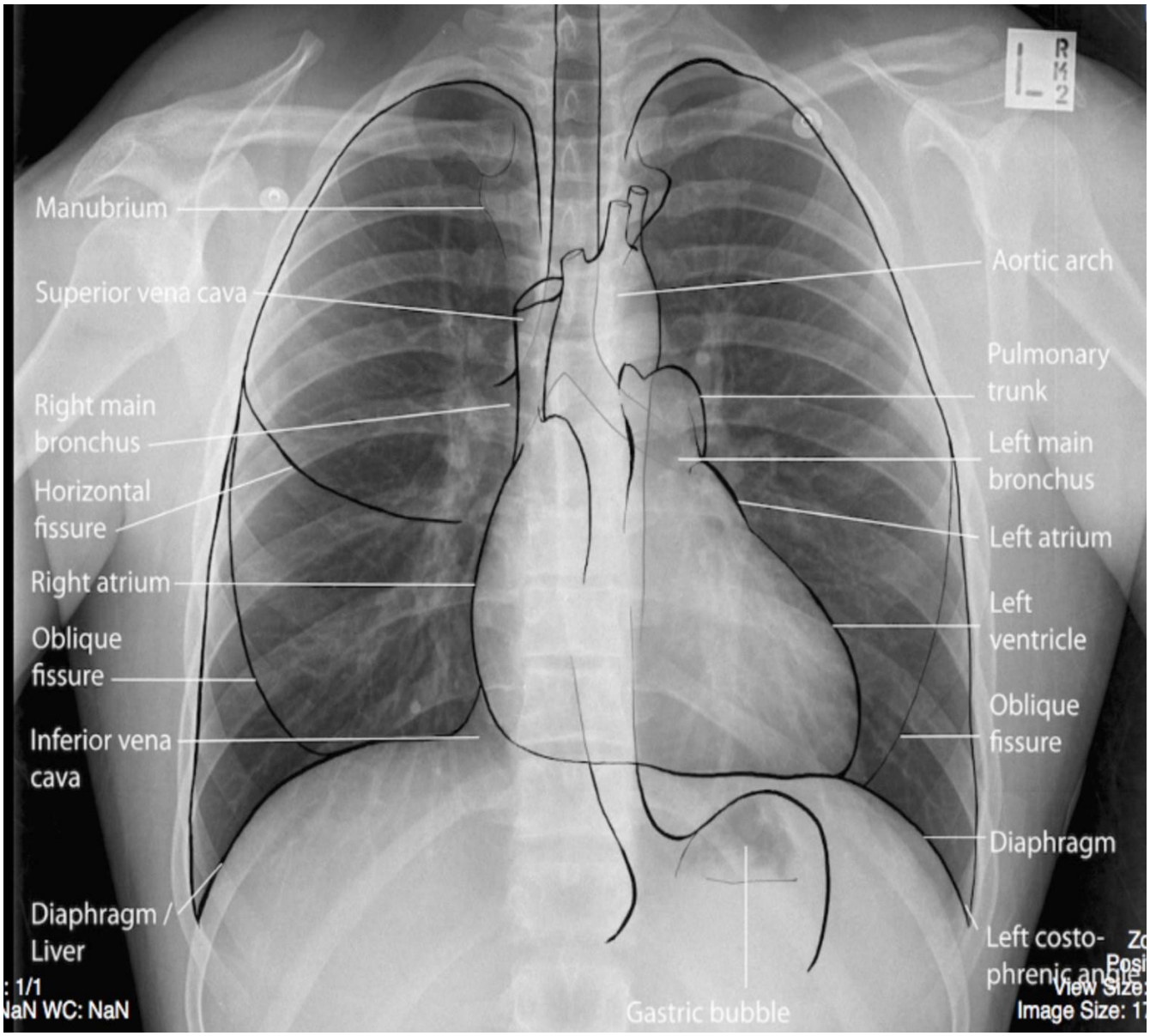
1.3.3: Systematic Approach

A systematic method to assess a chest x-ray is the ABCDE system, where A stands for evaluating Airways, B represents bones and soft tissues, C represents the cardiac mediastinum or silhouette, D represents the diaphragm. E represents everything else, including lungs and pleura. A systematic approach provides physicians with opportunities to identify common pathologies that chest x-ray is adequate to diagnose, such as pneumothorax, chronic obstructive pulmonary diseases, and pneumonia.

The above systematic method has been personally useful in image interpretation, and I have utilised it during my post-graduate university exams.

1.3.4: Anatomy of Chest X-ray

Several vital structures are visible in the chest x-ray; these are illustrated in figure 1.5 and figure 1.6.



Source: https://openpress.usask.ca/undergradimaging/chapter/chest/. creative commons licence -by-NC-SA 4.0 [42].

Figure 1. 5: Structures visible on a PA chest x-ray.

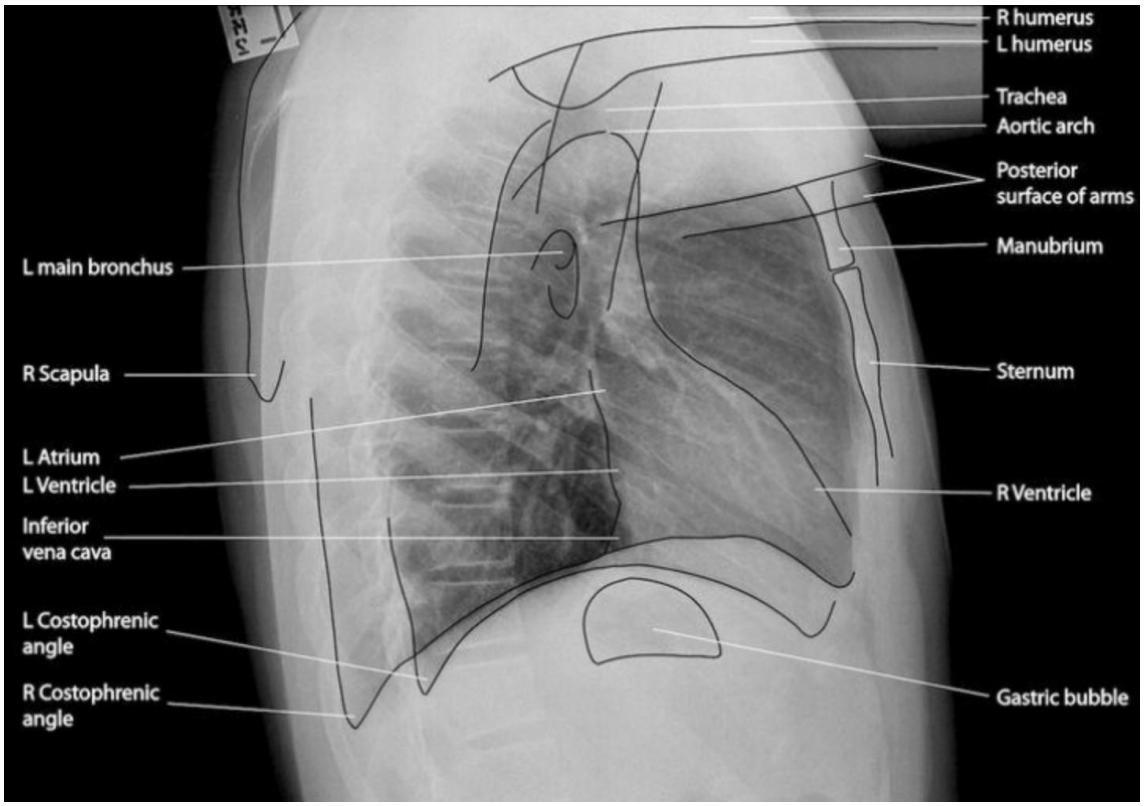


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Figure 1. 6: Structures visible on a lateral chest x-ray.

As illustrated above, image structures visible on chest x-rays are lung, heart, ribs, sternum, oesophagus, and spine; the pleura and fissures are typically not seen well [43-45].

In relation to the upcoming images, I would like to acknowledge that some chest x-ray and CT images are adapted with permission from Shulman, H. Harry's Chest Atlas, this used to visually demonstrate pathologies in which either the pathology or permission was not possible from the patients, and all his images are referenced as such[46]

1.3.4.1: A: Airways

The normal trachea is positioned centrally; it should be assessed for any deviation or obstruction. If the trachea is not centrally placed, it is crucial to determine if it is due to incorrect positioning or pathology.

If the trachea deviates, then the lungs' assessment is used to help distinguish between pneumonectomy, pneumonia, atelectasis, airway obstruction, and pleural effusion as the cause or this. For instance, a large pleural effusion causes displacement of heart or mediastinal structures away from the area of opacification, as illustrated in figure 1.7.

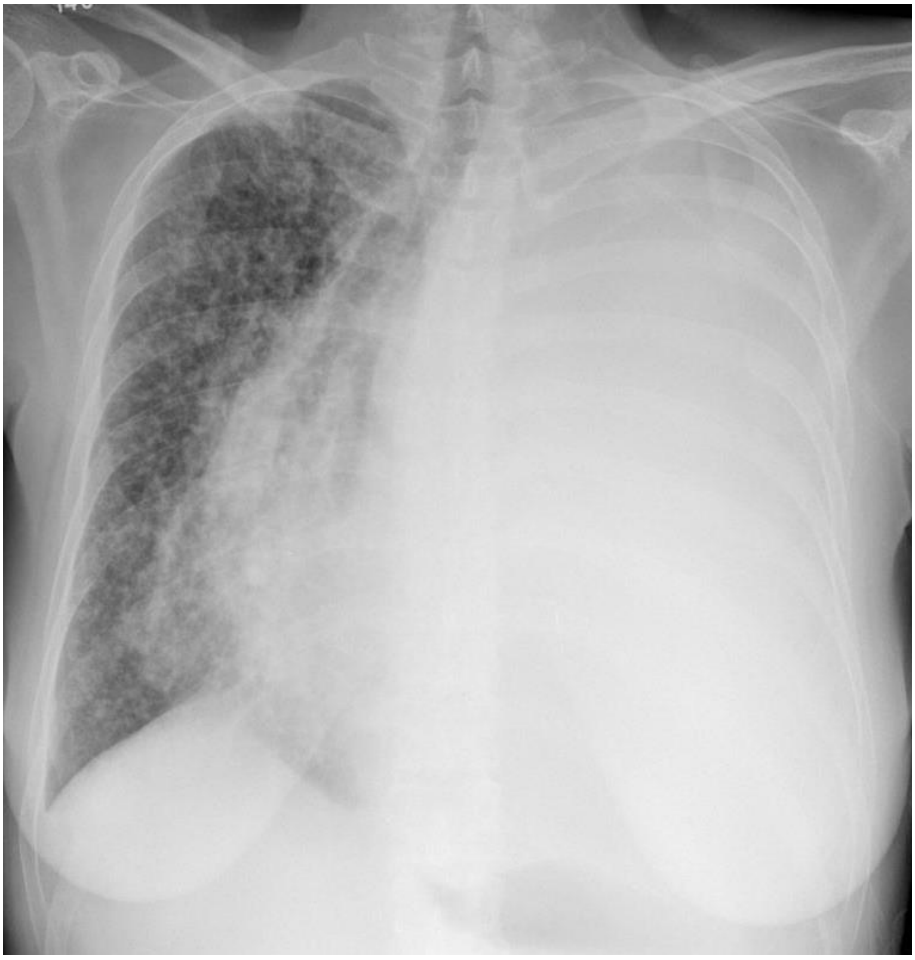

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Figure 1. 7: Large left side malignant pleural effusion, there is displacement mediastinal structures away from the point of opacification.

A large pleural effusion usually causes displacement of heart or mediastinal structures away from the area effusion; however, small effusion may not change any of the structures.

Conversely, with large atelectasis, a collapse of the entire lung with a displacement of the mediastinal systems and heart towards the side of atelectasis is typically seen[47]. Atelectasis is visually demonstrated in figure 1.8.

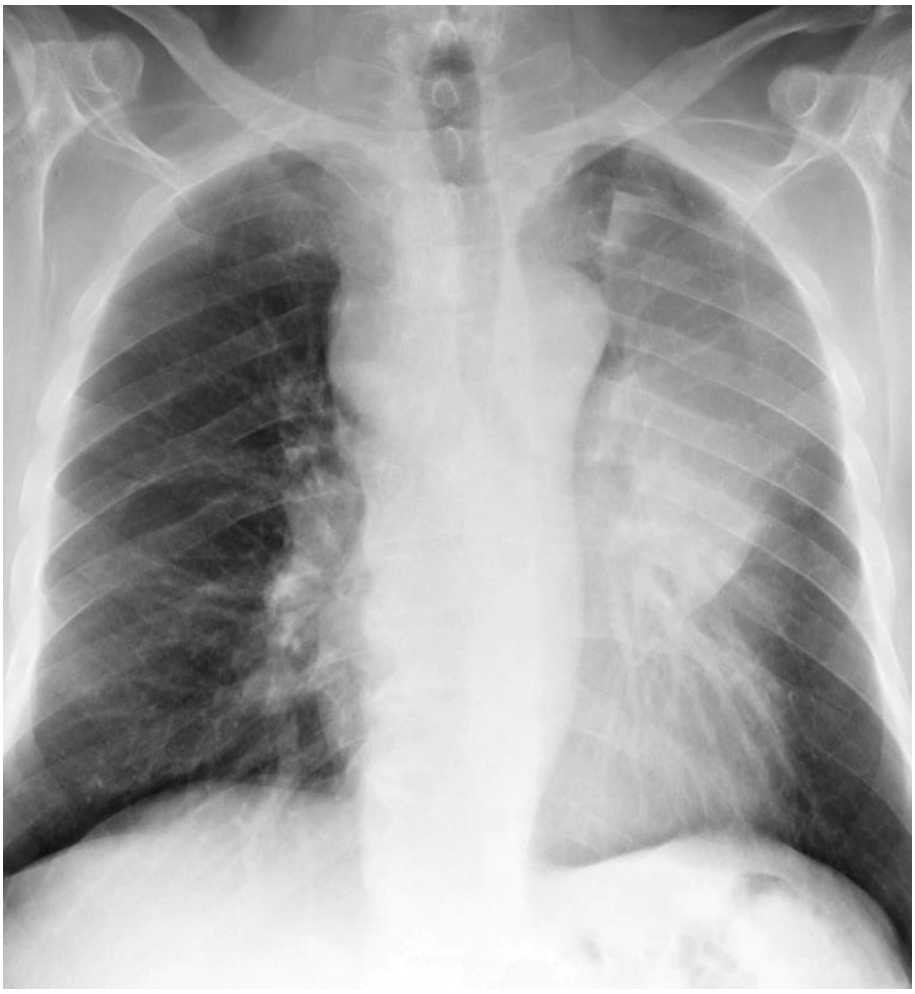

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Figure 1. 8: A shift of the trachea and mediastinal structures towards the left side in left upper lobe atelectasis.

In cases of pneumonia, mediastinal structures typically do not shift. However, air bronchogram and air space opacities and obscuration of silhouette boundaries such as the right para-tracheal stripe are prevalent, as illustrated in figure 1.9.

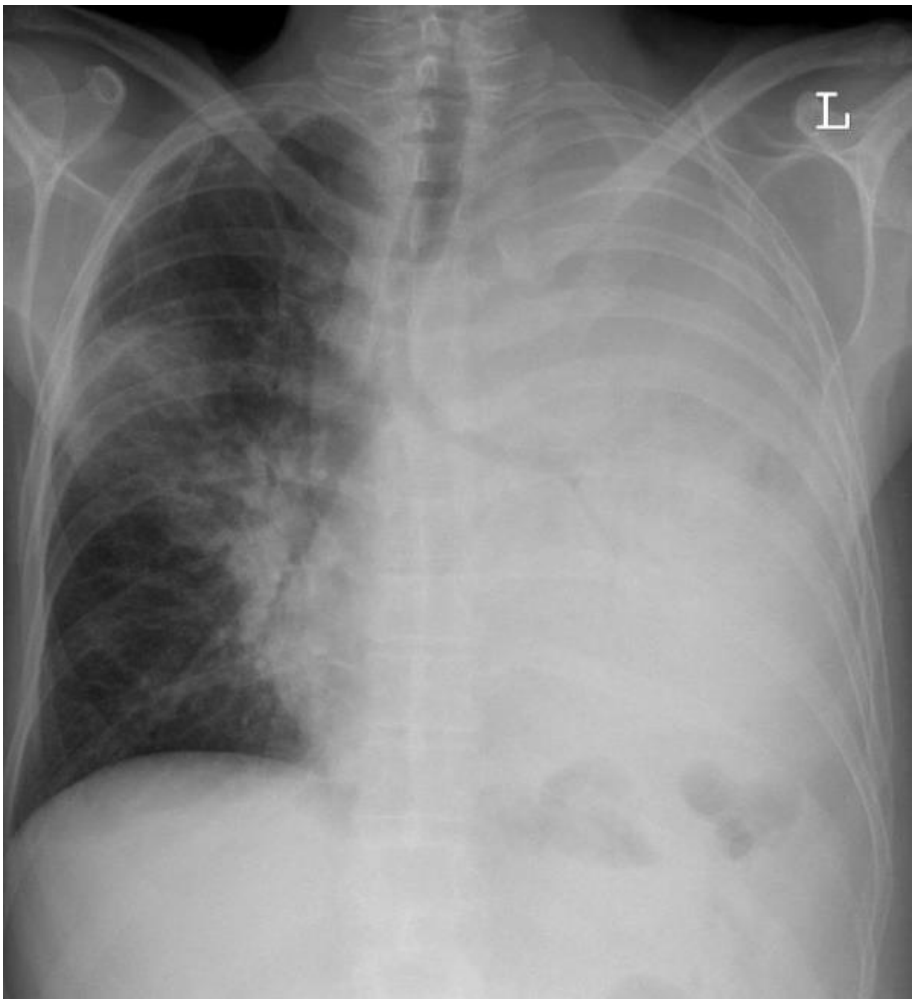

Figure 1. 9: Complete white out of the left lung with air bronchograms caused by pneumonia.

In pneumonectomy, opacification occurs as a result of fluid partially filling the space where the lung has been surgically removed. The heart and mediastinal structures such as the trachea shift towards the place of opacification, and lung markings should be absent in the area of the opacification.

1.3.4.2: B: Bones or Soft Tissue

Assessment of the bones visible on the chest x-ray involves reviewing the imaged upper humerus, thoracic spine, scapulae, clavicles, sternum, and ribs for fracture and uncommon pathologies such as bone metastases. Rib fractures can cause chest pain, and dyspnoea can present similar to PE; it is important to assess each rib and assess rib position, which can also be disrupted in occult fractures. The thoracic spine required assessment on lateral x-rays.

Assessment of thoracic wall soft tissue adjacent to the ribs in the axillary and imaged lower neck is important to exclude surgical emphysema that can occur after trauma or fractures ribs. Rare lesions such as large soft tissue tumours can also present on x-rays as masses.

1.3.4.3: C: Cardiac Silhouette and Mediastinum

The mediastinum encompasses the great vessels, pulmonary vessels, lymph nodes and the heart. Chest x-rays allow for the assessment structures separately. The important areas to review are the aorta-pulmonary window, aortic knuckle, and right para-tracheal stripe for the presence of pathology or enlargement.

1.3.4.4: Silhouette Sign

The silhouette sign describes the loss of a particular contour or border, for example, the heart border or the aortopulmonary window[48]. If the border or contour is obscured, this may be secondary to consolidation in this area or the adjacent lung, a mass or an enlarged node in the area.

1.3.4.5: Hila

The hilar structures encompass the lung pulmonary arteries and veins, the main bronchi, and lymph nodes. The left hilum is nearly always higher placed in comparison to the right hilum. Therefore, while undertaking a hila assessment, it is often vital to check their size, shape and position. The nodal structures are not seen in a normal hilum and only become seen with abnormalities. The following conditions are the common causes of hilar enlargement:

- Malignancy such as metastases from lung cancer, metastatic extrathoracic cancer such as breast cancer, or primary disease such as lymphoma can cause hila enlargement. Figure 1.10 below shows prominent bilateral hilar lymphadenopathy in patients with a history of lymphoma.
- Infections, such as bacterial pneumonia, tuberculosis or uncommon infections such as histoplasmosis
- Inflammatory conditions, such as sarcoidosis
- Pulmonary hypertension is a common cause of hilar enlargement[49].
- Congenital issues such as bronchogenic cysts or foregut duplication cysts can cause hila enlargement.

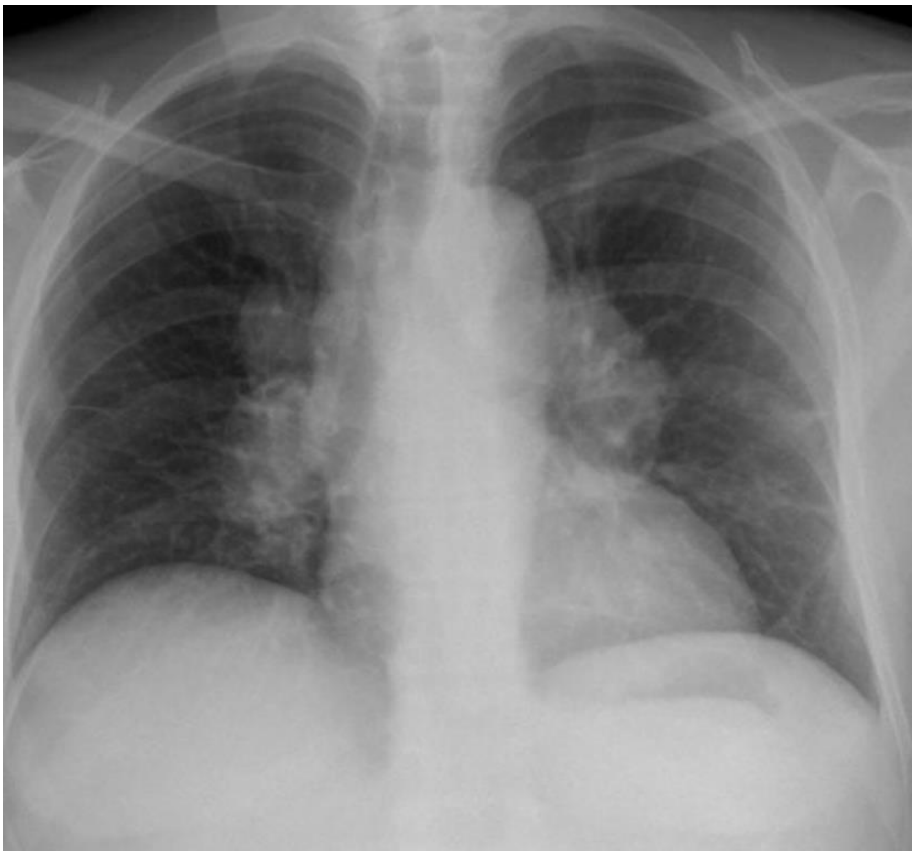

Figure 1. 10: Prominent bilateral hilar lymphadenopathies in patients with a history of lymphoma.

It is important to know that the hilar nodal structures are not seen in a normal hilum and only become seen with abnormalities such as malignancy or Inflammatory conditions.

1.3.4.6: Heart size

The heart's size is not measured directly; assessment is conducted with the cardiothoracic ratio (ratio between heart measurement and lung measurement on PA chest radiograph). This defines the heart as either enlarged when the cardiothoracic ratio is great than 0.5. However, the cardiothoracic ratio is inaccurate when care is not taken to measure through an approach widest portion of the heart or aerated lung on PA chest x-rays[50]. It is crucial to acknowledge that an AP chest x-ray may exaggerate heart size as a result of greater magnification. Therefore, it is recommended to use only a PA view for the assessment of cardiac enlargement. The most common cause of heart failure is left heart failure with hypertrophy and pulmonary oedema; a chest x-ray is very useful for the assessment of both.

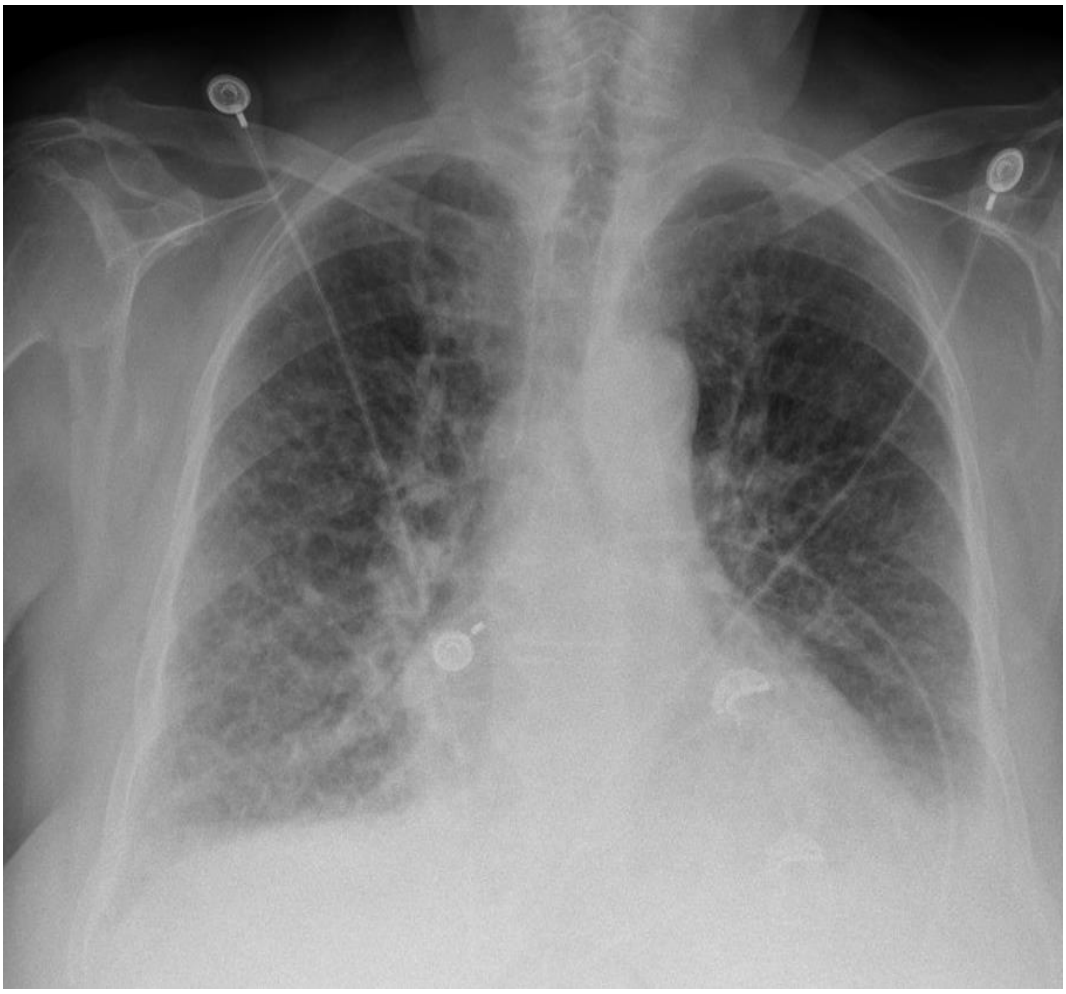

Figure 1. 11: An enlarged heart and prominent ill-defined lung markings suggest interstitial pulmonary oedema.

The most common type of heart failure is left heart failure; fluids start building within the lungs, known as pulmonary oedema, as shown above, which results in shortness of breath. Conversely, right heart failure, which most commonly occurs with severe left heart failure, causes a build-up of fluid in the abdomen, feet, and legs[51]. Figure 1.11 demonstrates heart failure and pulmonary oedema. Pulmonary oedema is the acute build-up of fluid in the lungs, and its radiographic findings are discussed below.

1.3.4.7: D: Diaphragm

Both sides of the diaphragm are assessed in terms of opacity, shape, position, and free gas underneath. The diaphragm opacity should be well defined; if not, then there may be overlying consolidation or atelectasis. If there is increased opacity similar to the bone, this may indicate pleural calcifications asbestos exposure. The diaphragm shape is occasionally distorted secondary to congenital defects, previous infection or surgery. In terms of position, the right diaphragm is usually higher than the left; the stomach gas bubble occurs in the left diaphragm. Free gas underneath the

diaphragm is an important finding as this can indicate perforation of a hollow viscus or recent surgery; this is illustrated in figure 1.12.

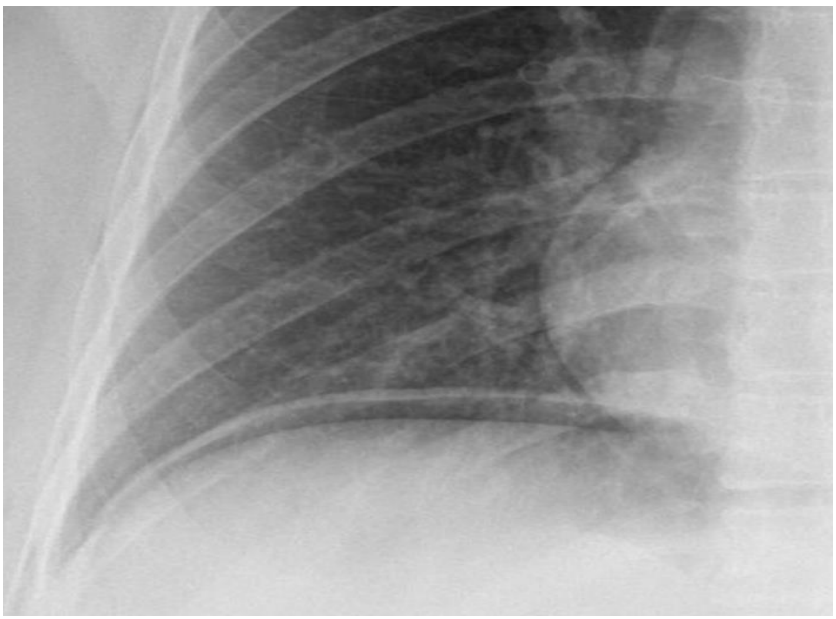

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Figure 1. 12: Gas under the diaphragm due to bowel perforation.

1.3.4.8: E: Everything Else (Lungs and Pleura)

It is often challenging to assess both lungs at one time. Lungs are separated into three zones that are upper, middle and lower zones. This permits the assessment of each section more precisely. Notably, the lower lung zones typically extend behind the diaphragm on a PA image since the lung passes behind the dome of the diaphragm.

The lung findings of pulmonary embolus on chest x-ray are uncommon and can be challenging to identify. These findings include peripheral opacification indicating an infarction or Westermark's sign that denotes blood flow redistribution with large pulmonary embolus Fleischner's sign which is widening of pulmonary arteries, is uncommon.

Each section's assessment separately can give us an opportunity to detect small, poorly defined opacity, as illustrated in figure 1.13 on the right middle lobe medially.

The most common lung pathologies and alternative diagnoses for pulmonary embolus can present in many patterns; this will be discussed separately in the next section.

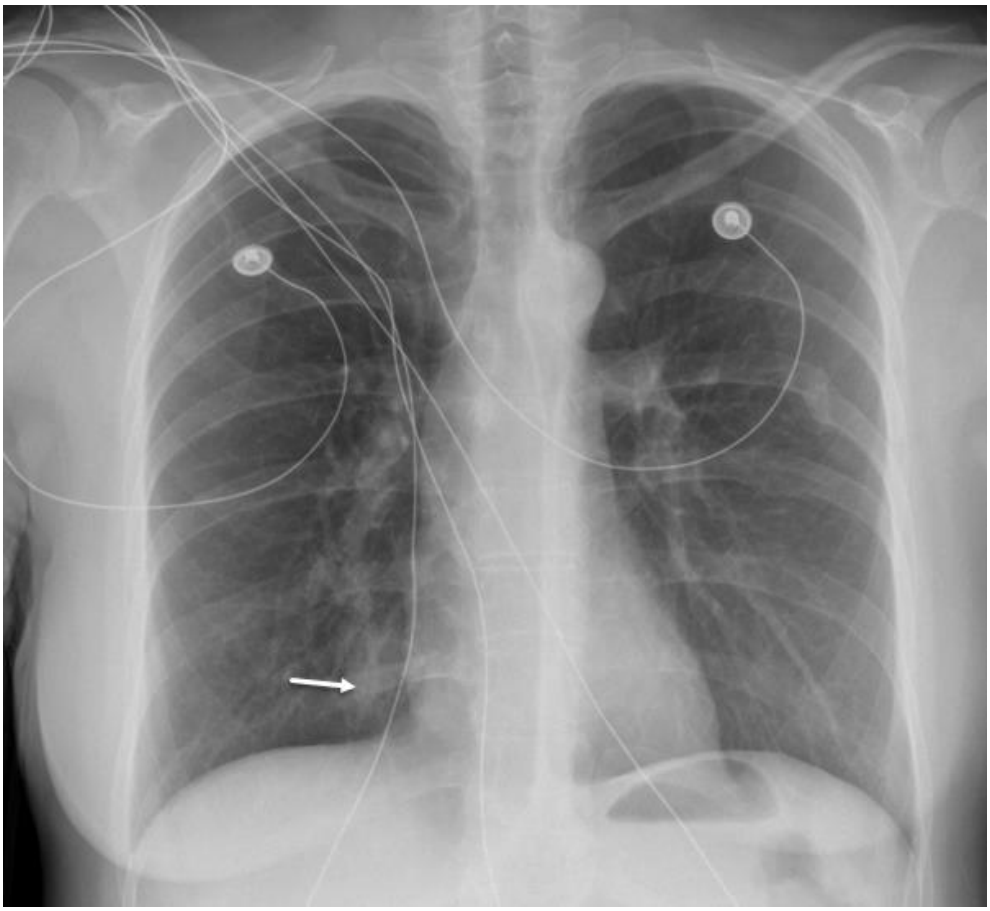


Figure 1. 13: A poorly defined opacity in the right middle lobe medially (arrow).

As illustrated above image, it is often difficult to assess both lungs at one time. Hence, separating lungs into three zones is upper, middle and lower zones, which permits the assessment of each section's assessment more accurately.

Pleura: The normal pleura is not seen on the x-ray. The pleural is only appreciated when it is thickened, calcified; the pleural space is filled with air (pneumothorax) or fluid (pleural effusion or haemothorax).

It is important to trace the pleura around the entirety of both lungs and in the fissures. Assessment for potential pleural effusion or thickening is required at the constropheric angles.

Occasionally masses occur in the pleura, such as lipoma, sarcomas and hemangiomas, or any chest wall bone neoplasms such as osteosarcomas. These are seen as focal smooth lesions on the pleura. The primary neoplasm of the pleura, mesothelioma, is caused by asbestos exposure and cause calcifications of the pleura with both pleural thickening and effusion. Hilar enlargement can also be seen with lung volume reduction.

Pneumothorax is a cause of dyspnoea and chest pain and can mimic pulmonary embolus. Therefore it is essential to ensure that lung markings are visible on the chest wall’s edge.

Pneumothorax may have hyperlucency encompassing the whole affected hemothorax but can be small or subtle, as in figure 1.14. Notably, the tension pneumothorax lungs may ultimately collapse, causing a mediastinal shift towards the opposite side.

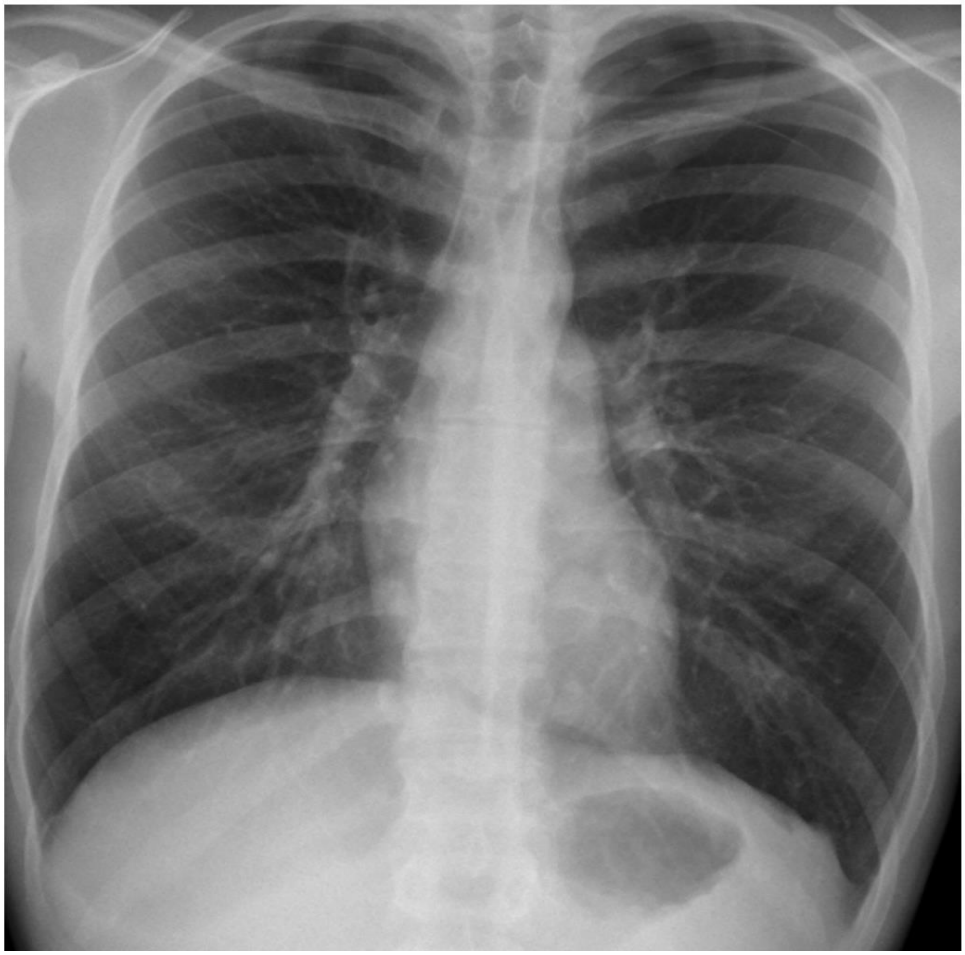


Figure 1. 14: Left upper lobe showing small pneumothorax.

It is vital to ensure that lung markings are visible on the chest wall's edge; there is a pneumothorax in the left upper lobe in the above case. It is also essential to avoid overlooking the hidden areas, including retrocardial zones, below the diaphragm and hila.

In summary, having adequate knowledge about chest image interpretation and using a systematic sequence similar to the ABCDE structure may decrease the CTPA overuse.

Understanding the differential diagnosis and disease patterns are discussed in the following paragraphs.

1.4: Section Four: Pulmonary Embolism Clinical Presentations

This section's main goal is to offer background information on Pulmonary Embolus (PE), including the source or origin of PE, the process of blood clot formation, imaging and the risk factors for pulmonary embolism. This section also discusses how PE signs and symptoms overlap with other acute respiratory diseases.

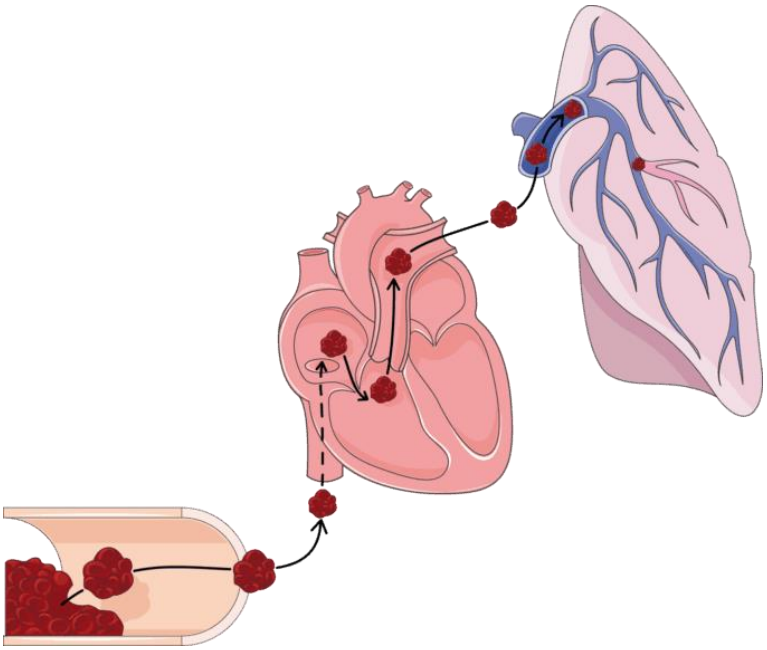
1.4.1: Definition of Pulmonary Embolism

Pulmonary embolism is a condition where a thrombus (blood clot) moves or embolises into the pulmonary arterial system. PE is a serious condition and stands as one of the most prevalent cardiovascular ailments among hospitalized patients[52].

The percentage of PE diagnosis in patients going through CTPA was 11% in this imaging department in Canberra.

1.4.2: PE Pathophysiology

Blood coagulation or clotting may be defined as the process that helps avoid excess bleeding when there is an injury to the blood vessels. Platelets and multiple clotting proteins within the plasma form a plug together to stop bleeding; this plug is initially soft and covers the point of injury. Fibrin, a blood protein, further strengthens the platelet plug, and ultimately, a solid clot is formed at the site of injury, after which healing can take place. Remarkably, after the injury, the human body is able to dissolve the blood clot formed after the healing of the injured wall. Occasionally the formed clot in the blood vessels may not physiologically stop forming or dissolve, resulting in the clot increasing in size or propagating. A blood clot that is abnormal or large may inhibit blood flow through the vessel and is called a thrombus. An abnormally large clot or thrombus is more likely to break off/embolise, move to the inferior vena cava, and ultimately travel through the right heart and then embolise to the pulmonary artery illustrated in figure 1.15.



Source: https://smart.servier.com/smart_image/pulmonary-embolism/ server creative commons[38].

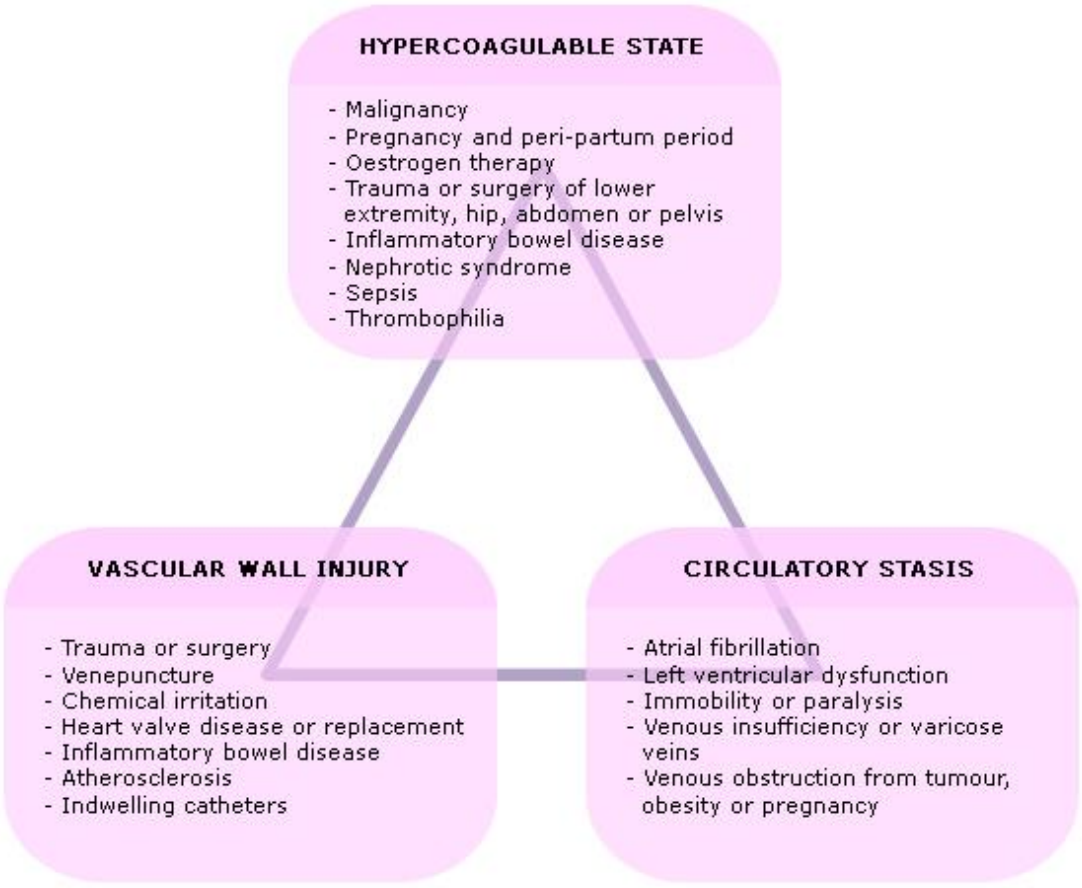
Figure 1. 15: Clot-forming processes; thromboembolism usually forms when the clot cannot dissolve naturally.

1.4.3: Pulmonary Emboli Sources

PE emerges from the systematic veins, with the majority due to a thrombus with the pelvic vein or lower extremities' deep veins[53-56]. In most cases, the thrombus arises in the pelvic veins because of predisposing factors such as immobility, current pelvic surgery, vascular devices, pelvis infection or pregnancy. It may also arise from the upper extremity as a result of cardiac device insertion or central venous catheters. In rare cases, amniotic fluid or air can also embolise, fat embolism occurs when fatty acids originating from a fracture of a bone embolise to the lung causing chemical injury to the lung[57].

1.4.4: Pulmonary Embolism Risk Factors

As PE is secondary to deep vein thrombosis, abbreviated as DVT, the risk factors for DVT require consideration. The major risk factor leading to DVT is slowed blood flow, also called stasis which can be caused by prolonged bed rest, hospital stays, long flights, and car trips. Other important risk factors are hyper-coagulation due to hormonal medications such as oral contraceptives, pregnant patients, and patients with genetic blood clotting conditions such as factor IV Leiden and hypercoagulability in acutely unwell patients or those patients undergoing surgery from inflammation. Vessel or endothelial injury also caused an increased risk of DVT, such as in smoking, trauma and surgery. Most patients who develop DVT have several risk factors[50]. The risk factors for DVT, namely stasis, hypercoagulation and endothelial injury, are classically called 'Virchow's Triad' and are illustrated below.



Source: https://www.rcemlearning.co.uk/reference/deep-vein-thrombosis/#1568729656062-fc7bc64c-6a60, Royal College of Emergency Medicine, permitted under the "fair use" provisions of the Copyright [58]

Figure 1. 16: Stasis is the main factor that can cause a pulmonary embolism.

1.4.5: The Physiological Effect of PE

PE can be a life-threatening disorder. The coexisting cardiopulmonary ailment, clot location, size, hypoxic vascular response, and emboli resolution rate determine the severity of pulmonary embolism. Massive PE results in severe symptoms such as cardiac failure, deoxygenation or sudden death. When the obstruction is less than 20% of the pulmonary arteries lead to minimum hemodynamic instability since the pulmonary vessels can compensate[49]. When the obstruction is below 40%, there is a modest escalation in the right ventricle's workload; the cardiac output is, however, maintained by raising the cardiac contractility and heart rate. When obstruction surpasses 50% or more, there tends to be a failure in the compensatory mechanism with right arterial pressures rising and cardiac output decreasing; ultimately, failure can occur with deoxygenation and lactic acidosis developing. In high-grade acute pulmonary embolism obstruction, systematic failure can emerge with cardiac output falling precipitously with possible sudden death[59].

In most cases, in patients with no history of cardiopulmonary ailments, the right ventricle may produce the required pressure to overcome any escalation of pulmonary vascular resistance by the

embolism. Nonetheless, patients with pre-existing cardiopulmonary ailments have reduced pulmonary vascular reserve and even moderate PE may result in considerable hemodynamic instability.

1.4.6: Oxygen Exchange Abnormalities

Hypoxia is a deficiency of oxygen that reaches the tissue. This is the most common physiological outcome of pulmonary embolism. Pulmonary embolism induces hypoxia but initially reducing available blood for oxygenation, called a ventilation-perfusion mismatch. Pulmonary embolism may eventually cause cardiopulmonary failure from obstruction that furthers hypoxia.

Furthermore, ventilation-perfusion mismatch also causes blood redistribution to the non-occluded vessels from the occluded pulmonary artery resulting in some compensation[60].

1.4.7: Prevention

Effective practices to avoid DVT and PE include staying active while on a long trip, exercising regularly, and reducing immobility. High-risk patients may require secondary prevention with compression stocking, blood thinners and early mobilisation after surgery.

1.4.8: Management of Pulmonary Embolism

Heparin-based anticoagulants are the most effective PE treatment. These drugs aim to break down the thrombus, prevent reoccurrence of thrombus and reduce emboli propagation. They are available in a variety of preparations, with the most commonly used being low molecular weighted heparin or intravenous unfractionated heparin. Furthermore, other treatments utilized include Warfarin and rivaroxaban[49, 61]. Patients who have cardiovascular compromise or who deteriorate despite anticoagulation treatment may require further treatment such as interventional reperfusion or fibrinolysis[62].

1.4.9: What if Patients Cannot Take Blood Thinners

High-risk patients who cannot take blood thinners or those patients with a very high risk of DVT/PE should have inferior vena cava filter placement; this prevents the clot from the lower leg embolising to the lung[63].

1.4.10: Clinical Diagnosis of Patients with Suspected PE

PE diagnosis is always challenging because its symptoms are unspecific and may be found in many other cardiac and acute respiratory ailments. The following sections discuss the approach to diagnose PE and methods to differentiate PE from other respiratory ailments that cause shortness of breath and chest pain. This section will also discuss some aspects of clinical testing.

1.4.11: Clinical Presentations in PE

In the emergency department, patients presenting with PE can present with a wide variety of symptoms, with the most common symptom being shortness of breath and chest pain. Patients can also be asymptomatic, with PE diagnosis being made incidentally on imaging for other purposes.

When patients present with these signs, the most effective approach is to distinguish pulmonary embolism from other ailments via history and physical examinations prior to another testing. When patients are presented to an ED with respiratory distress, physicians need to take a careful/detailed history and an appropriate physical examination targeting differentiating the alternative cause of PE.

In the emergency department setting, other entities that can have similar signs and symptoms as pulmonary embolism are: pneumonia, asthma, myocardial infarction, pneumothorax, atelectasis, oesophageal dysfunction, rib fractures, pleural effusion and cancers. In the current epidemic, coronavirus can also present with shortness of breath and chest pain which may mimic PE [64, 65]. It should also be noted that in the emergency setting, heart failure, exacerbation of chronic obstructive pulmonary diseases and pneumonia is considered the most common acute ailments that cause cardiopulmonary symptoms like PE. Some studies have found that more than 20 diseases occur at least as frequently as pulmonary embolism [66, 67].

Signs and symptoms offer crucial information regarding PE. The most common symptoms in the PIOPED II trial were dyspnoea(73%), pleuritic chest pain (44%), calf/thigh pain (44%), cough (34), tachypnoea(45%), tachycardia (24)[68]. Other less common symptoms were: haemoptysis (13%), wheezing (21%), and orthopnoea (28%)[69, 70]. These trials also found that symptoms are insignificantly in some patients, and pulmonary embolism can be asymptomatic.

The following section will discuss the common symptoms of PE in greater detail, namely pleuritic chest pain, dyspnoea, tachycardia, cough, sputum, haemoptysis, tachypnoea and hypoxaemia.

1.4.12: Pleuritic Chest Pain

Pulmonary embolism is one of the most common causes of pleuritic chest pain, characterised as sudden intense sharp or burning pain on inspiration or expiration. Chest pain is also common in other diseases besides PE. It is essential to identify the nature of chest pain; for instance, the type of chest pain can be crushing, burning, aching, or stabbing. The actual location of the pain, its duration, onset rate, severity, as well as relieving factors and associated features such as sweating, vomiting, and nausea, amongst others, are important in differentiating PE from other cardiopulmonary diseases [71, 72].

For instance, pleuritic pain resembling knifelike pain that can be localised by one fingertip radiating to the lower extremities is likely to have a cardiac origin[73]. On the other hand, sharp pleuritic

chest pain that gets worse in inspiration or expiration is a frequent clinical sign among patients with suspected PE. Other causes are rib fractures, muscular injury or strain, malignancy, empyema, and pneumothorax[74].

Although chest pain tends to be common among patients with suspected PE, various conditions can cause it, as shown in table 1.2 and table 1.3. This has been discussed by several authors [73, 75], [76].

Table 1. 2: Conditions that can cause chest pain.

Cardiovascular diseases	Pulmonary diseases	MSK and others	Gastrointestinal(GI)
Pericarditis Myocarditis Aortic dissection Acute coronary syndrome Aortic stenosis Heart failure	Pneumothorax. Pulmonary embolism Asthma Pneumonia Lung cancers	Costochondritis Rib fractures Psychiatric, e.g. Panic attack	Oesophagus inflammation/ diseases Stomach ulcers

Table 1. 3: The four most common conditions that cause chest pain.

	Pulmonary embolism	Aortic dissection	Pneumothorax	Acute coronary diseases
Chest pain main symptoms	Acute onset of dyspnoea with pleuritic sharp pain. Tachycardia and tachypnoea.	Acute onset chest pain radiating to back, tearing, ripping pain.	Acute onset not radiating but sharp and pleuritic. Abrupt onset of SOB and chest pain.	Acute onset substernal chest pressure, burning/heaviness pain radiating down arm to jaw, neck, shoulder, and arm.

1.4.13: Dyspnoea

Dyspnoea is a medical term that refers to shortness of breath or difficulty in breathing. Dyspnoea in PE is related to the ventilation abnormality associated with vascular obstruction. It also describes the feeling that a patient experiences when they are forced to utilize an extra effort in breathing. The best method to differentiate conditions that cause dyspnoea is to classify them on the drivers of the effect of the dyspnoea, namely the presence of hypercapnia, hypoxia and reduced oxygen delivery; this is demonstrated in table 1.4.

Table 1. 4: The common cause of acute dyspnea[74].

Hypoxemia	Hypercapnia	Less O2 delivery
Pulmonary embolism Pneumonia Pleural effusion COPD Pulmonary oedema	Asthma COPD Other diseases, such as acute neurological diseases	Massive PE. Heart failure, coronary artery diseases Tension pneumothorax. Airway obstruction, infection or anxiety

Various cardiovascular and pulmonary ailments may result in dyspnoea. The prevalent pulmonary diseases causing dyspnoea include interstitial lung disease, pleural effusion, COPD, and asthma. The cardiovascular diseases that can cause dyspnoea include coronary artery diseases, valvular disorders, heart failure, pericarditis, and cardiac conduction disorders[77]. Dyspnoea may also be caused by obesity, neuromuscular diseases, and severe anaemia. The most frequent conditions causing dyspnoea are heart failure and COPD[49].

In some cases, the cause of dyspnoea can be predicted based on the timeframe, for instance:

- Abrupt dyspnoea is typically common in PE, acute exacerbation of asthma and pneumothorax. Acute dyspnoea is the most common symptom in massive PE; it is found amongst 86% of the patients with massive PE [49].
- Longstanding dyspnoea for days or weeks is most often due to cardiac failure, pneumonia, or asthma exacerbation.
- Ongoing dyspnoea for months is usually seen in pulmonary fibrosis.
- Ongoing dyspnoea for years is commonly seen in COPD.

1.4.14: Tachypnoea

Tachypnoea is described as abnormal quick breathing associated with a respiratory rate that is over 30 breaths every minute, which is a significant PE indicator. The common conditions that cause tachypnoea are:

- Interstitial lung ailments such as carcinomatosis, lymphangitis, and pulmonary oedema
- Pulmonary vascular ailments, for instance, pulmonary hypertension and PE.
- Psychiatric sicknesses, such as anxiety and panic diseases
- Neurovascular, for example, brain disorders and muscle weakness [78].

1.4.15: Cough

PE symptoms, including cough, can vary greatly depending on the extent of the involvement burden of pulmonary blood clots. In some cases, patients with PE experience a dry cough. However,

cough is non-specific and can be found in many conditions, including chronic rhinosinusitis, gastroesophageal reflux, and asthma. Contributors to acute cough include viral infections, acute bronchitis, and pneumonia. Conversely, the contributors to a chronic cough that lasts over weeks are multi-factorial and common causes include post-nasal drip, gastroesophageal reflux, asthma, viral infection and occasionally sinister pathology such as lung cancer. A cough with haemoptysis is particularly troubling and may indicate lung cancer, particularly in smokers [79]. Cough is frequently present and seen in 53% and 52% of patients with massive and submissive PE, respectively[74].

Cough associated with sputum is frequently seen in conditions such as bronchitis and pneumonia. Conversely, dry cough is most common in interstitial lung diseases and asthma; however, if it is associated with fever, it may further reveal the presence of COVID-19. Other conditions in which patients may experience cough are:

- Laryngitis which presents as an acute cough associated with a hoarse voice.
- Pulmonary oedema which has a cough with clear sputum that worsens upon lying down.
- Asthma which has a chronic cough that becomes extreme after exercise.

The character of the sputum can also help differentiate the cause of the cough. For example, cough with sputum that is clear and white in colour is frequent amongst cigarette smokers. Green and yellow sputum is most probably initiated by inflammatory cells and can reveal an infection. The more common characterisations of sputum are:

- Pink/frothy is frequent among patients with cardiac failure.
- Offensive and green are common in bronchiectasis and abscesses.
- Grey/white is common in bronchiectasis and bronchitis.
- Grey/white is frequent among smokers.
- Yellow and extremely sticky is frequent on asthma
- Rusty and sticky are frequent on pneumonia infection[74].

1.4.16: Haemoptysis

Patients suffering from PE may experience some haemoptysis despite it being rare; this can also indicate the presence of PE complications such as pulmonary infarction. Only 13% of patients with pulmonary embolism experienced haemoptysis within the PIOPED II trial[31]. Also, coughing up blood may differ from streaks to massive life-threatening haemoptysis. Furthermore, haemoptysis ought not to be confused, for instance, with blood emerging from the GI tract or upper respiratory tract. Once it is determined that blood is not originating from elsewhere, physicians should assess the nature, frequency, colour, and amount of any associated sputum. Frequent contributors to haemoptysis are

pulmonary vasculitis, pulmonary embolism, bronchiectasis, bronchitis, lung cancers. Haemoptysis is rare among patients with submassive pulmonary embolism[49].

1.4.17: Tachycardia

Tachycardia is an increase in heart rate from baseline, and if it is unexplained, it may suggest possible acute PE. Tachycardia is clinical consideration when diagnosing PE and also risk assessment based on Wells' criteria; it is often present, but again non-specific; it is usually present in other cardiopulmonary diseases. Tachycardia is a significant symptom in approximately 38% and 8% of the patients suffering from a sub-massive and massive pulmonary embolism, respectively. Swollen calf, calf pain, increased rales, and crackles have been the clinical signs that are most often present with tachycardia in PE[49, 80].

1.4.18: Respiratory and Circulatory Examinations

When patients present with respiratory distress, physicians examine patients to collect valuable information to diagnose the underlying issue and therefore direct the treatment. The chest examination entails physicians assessing the air entry, chest expansion, and breathing sounds. For example, wheezing is common in heart failure, COPD, and asthma. Lung crackles are frequent in bronchiectasis, fibrosis, and pulmonary oedema. Difficult breathing, fast heart rate, fever, and cough reveal pneumonia or chest infection[81]. The most common findings on chest examination for patients present with PE is a normal examination; examination findings are usually seen in patients with sub-massive and massive PE.

1.4.19: Blood Tests and Imaging

The initial blood test that physicians usually send is an arterial blood gas examination to determine the adequacy of oxygenation; this is a reliable test in measuring blood oxygenation and is qualitatively different from oxygen saturation that is measured by pulse oximetry. Also, the clinician send-off the troponin test for cardiac issues; however, this can also be raised in massive PE. Further tests such as C-reactive protein (CRP), full blood count and blood chemistry may provide supplementary information concerning the cause of shortness of breath. Full blood count testing can provide evidence of infection of inflammatory disorders. Blood chemistry can help the renal issue; this is important prior to contrast administration.

Where a cardiac cause is suspected, it is suggested to undertake an ECG or an echocardiogram to exclude cardiac issues [82].

When there is clinical suspicion for PE but a low probability of PE on probability testing, D-dimer testing is conducted to identify if further imaging is required. This modifies the risk. The low probability

setting where the D-dimer is increased indicates an independently increased probability of PE[83-85]. Although increased levels of D-dimer are common in most patients with pulmonary embolism, it is non-specific and present amongst a larger number of other conditions such as during the postoperative period, advanced age, trauma, pregnancy, infections and inflammation, and among others patients with a cancer history. Although D-dimer is characterised by having good sensitivity and negative predictive value, it should be aware it has poor specificity when the above conditions are present.

However, the combination of both the increased D-dimer level and clinical suspicion permits additional imaging tests like CTPA. Conversely, normal D-dimer level and low clinical suspicion safely exclude pulmonary embolism [62, 86]. Likewise, it has been discovered that a normal D-dimer level effectively rules out PE, especially among younger patients[87]. In pregnant patients, D-dimer alone should not be utilized to exclude pulmonary embolism since it is raised in most pregnant patients[88]

1.4.20: Probability Testing

Emergency department physicians should perform PE probability testing after undertaking a history and physical examination. The most common utilized pre-test probability for pulmonary embolism is the Wells' score, illustrated in table 1.5.

Table 1. 5: Wells' model for determining the clinical possibility of PE[89].

Clinical features	Scores
Symptoms of DVT and leg swelling	3
Heart rate >100beats / min	1.5
Immobilization> 3 days or surgery in 4 days	1.5
Previous PE, or DVT	1.5
Haemoptysis	1
Cancer history	1
PE is likely or more likely than alternative diagnosis[31/97].	3

In the above table, a score below two represents a low likelihood for PE. Two to six represent a modest probability of PE, whilst a score of over six indicates a high probability of PE[90].

The following section discusses the most common next step in inpatient management, namely imaging.

1.5: Section Five: Imaging Pathways for Pulmonary Embolism

This section's main goal is to offer background information on pulmonary embolus main imaging modalities and why CT pulmonary angiogram stands as the ideal imaging modality.

Imaging pathways

Patients with suspected PE should have a history, physical examination, pre-test probability and the D-dimer test. D-dimer should not be used in isolation as several conditions and diseases can cause elevation, such as inflammation, infection, pneumonia, pregnancy, ruptured aneurysm, dissection, stroke, and heart disease. Other common causes include bruises or burns, trauma, surgery, and cancers.

Patients with low clinical suspicion for PE and negative D-dimer test should avoid having unnecessary imaging.

When there is clinical suspicion for deep venous thrombosis, an ultrasound assessment is indicated. If the ultrasound is positive, patients should start treatment that is the same as for PE; If the ultrasound is negative and there are chest symptoms, it is recommended to undertake a chest x-ray as the initial imaging modality. When there is no alternative chest pathology, a low dose of CTPA is more sensitives and specific than a ventilation-perfusion scan and should be used when there is a high suspicion for PE based on clinical history, examination and D-dimer[91].

1.5.1: Imaging Pulmonary Embolism

1.5.1.1: Aim of imaging

Imaging aims to identify if a patient has a PE before commencing treatment or to assess for another cause of chest pain and dyspnoea.

1.5.1.2: Advantages and Limitations of PE Imaging Modalities

1.5.1.3: Plain Radiography

A chest x-ray is used as initial imaging in patients with suspected PE. It continues to enjoy a significant role in the initial diagnostic imaging assessment. It is used to avoid the necessity for further imaging by revealing an alternative diagnosis, primarily acute respiratory illness, such as pneumonia or pneumothorax. The most frequent radiographic features include the peripheral opacification and Westermark sign representing the pulmonary haemorrhage consolidation that acts as a pulmonary infarction termed Hampton's hump. Usually, a chest x-ray is normal or inconclusive; however, as illustrated in figure 1.17, a chest x-ray can show consolidation, which is pulmonary infarction.

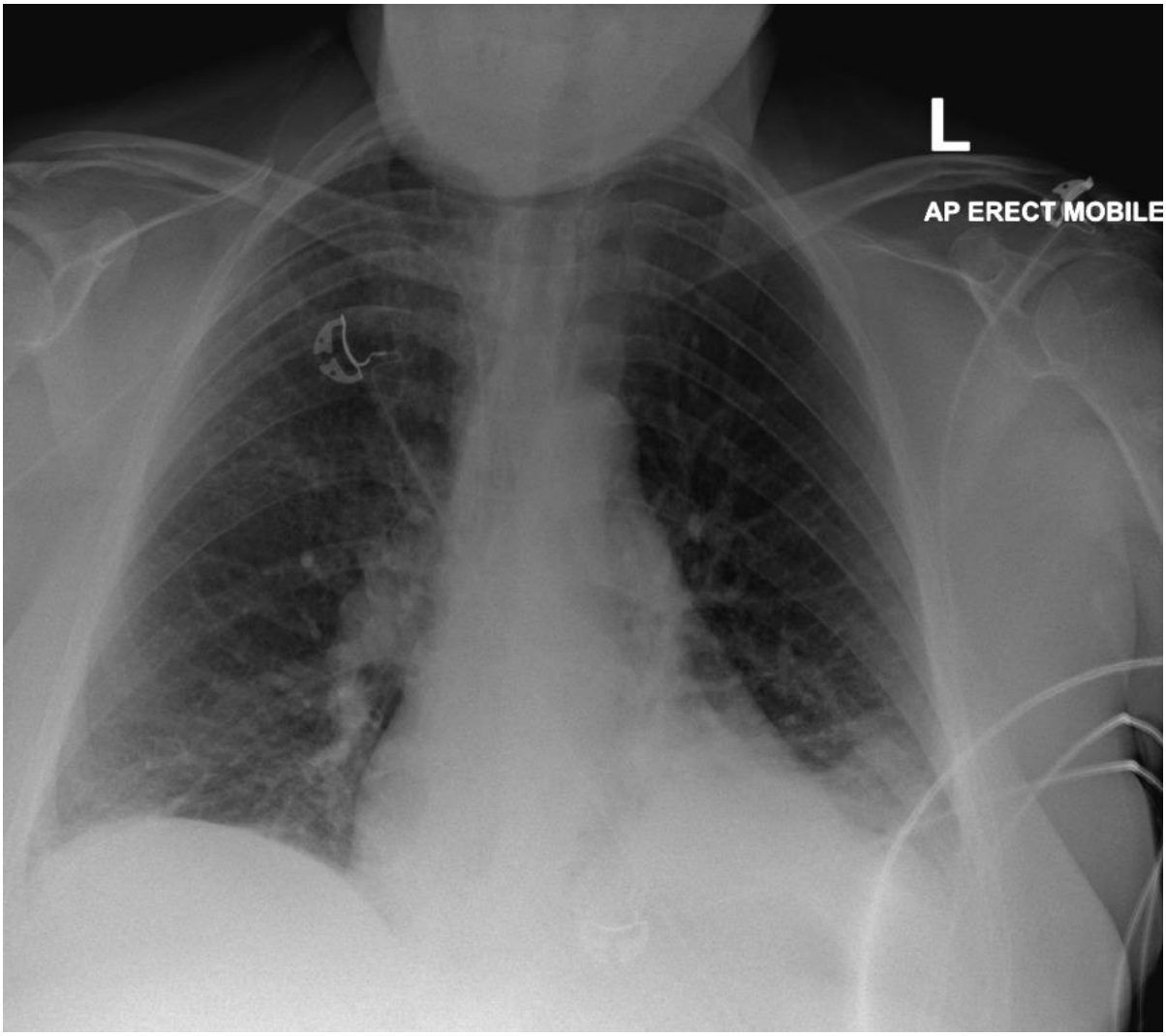


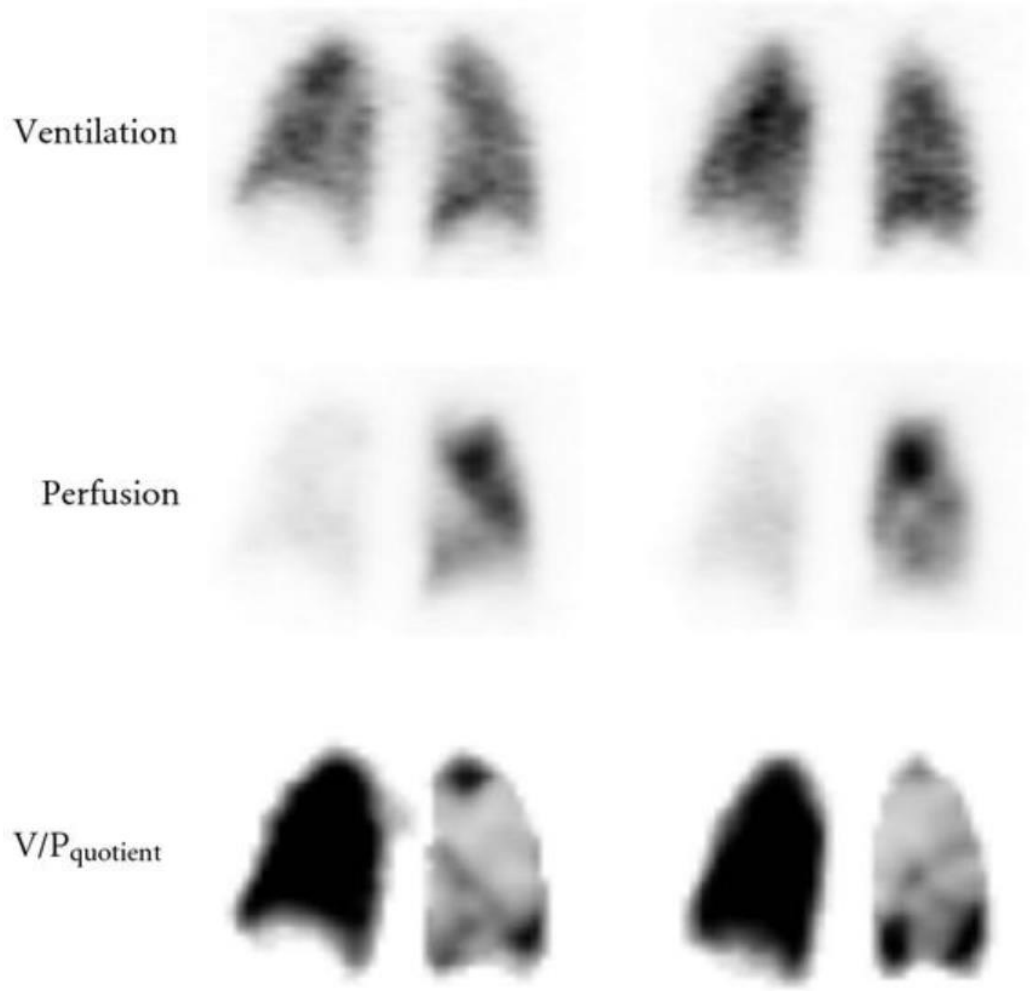
Figure 1. 17: Patient presented low oxygen saturation down, there is consolidation on the left lung base, which is due to pulmonary infarction.

The findings of the above chest x-ray were pulmonary consolidation at the lung bases with small pleural effusions. A further low dose CTPA examination is illustrated in figure 1.35 revealed bilateral PE.

1.5.1.4: Ventilation/ Perfusion (V/Q scan)

V/Q scan can be described as a non-invasive technique for assessing pulmonary circulation. It utilises ionising radiation in the form of radionucleotides[92]. It is considered imaging of choice for pregnant patients, obese patients and patients with renal failure or allergic to iodine. V/Q scan in the majority of patients with these few exceptions is no longer the initial diagnostic imaging of choice. If it is inconclusive, then patients may undergo a further CTPA when there is a strong clinical possibility of pulmonary embolism[69, 93]. The mean effective maternal dose is 1-2.5mSv, breast dose is 0.98-

1.07mGy, the foetal dose is predicted at 0.32-0.74 mGy[94]. Figure 1.18 visually demonstrates massive PE, as illustrated by Bajc and Jonson(2011)[95].



Source: https://www.hindawi.com/journals/ijmi/2011/682949/[95]

Figure 1. 18: Patient with massive PE. Absent perfusion in the right lung is seen, and subsegmental defects in the left are delineated in $V/Q_{Quoteint}$ image.

1.5.1.5: Ultrasound

Ultrasound is a simple, non-ionising and fast modality for the assessment of soft tissues and blood vessels in patients with suspected deep venous thrombosis. The Australian and Zealand College of Radiologists found that it is negative approximately 90% of the time in pregnant patients[96]. Therefore, it is not recommended to use ultrasound as the initial-line imaging modality when patients present with possible PE, except when patients reveal signs and symptoms linked with DVT. When DVT is diagnosed, then no further assessment for PE is needed. The figure below demonstrates DVT.

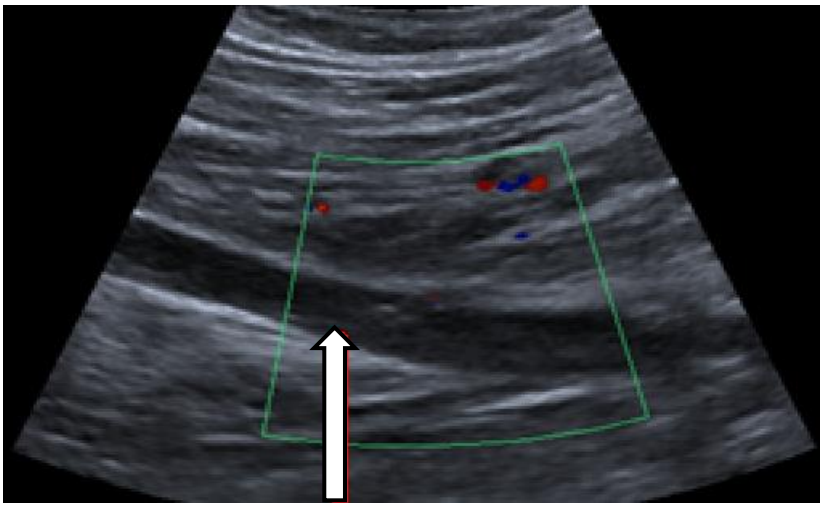


Figure 1. 19: Thromboembolic disease of deep venous thrombosis, arrow head.

The typical appearance of a DVT on doppler ultrasound is lack of flow in the expected direction, a non-compressible venous segment, pain on examination and increased venous diameter.

1.5.1.6: Magnetic Resonance Angiography (MRA)

Magnetic resonance angiography (abbreviated as MRA) is an imaging modality that is less commonly used in emergency departments. It is an appealing alternative imaging modality to CT for the examination of PE, especially in pregnancy, because it involves no ionising radiation. However, MRA has a high percentage of inconclusive findings, motion artefacts, and poor opacification, leading to more imaging and limited capacity to diagnose subsegmental branches. An alternative diagnosis is also not possible to identify [97].

According to Jones and Wittram, 25% of the MRA studies done in patients with suspected PE were technically inadequate, causing an unacceptably low sensitivity rate of 57%[98]. Hence, before adoption into common clinical practice, further advances in technology and techniques are required.

1.5.1.7: CT Pulmonary Angiogram

A low dose of CT pulmonary angiogram stands as the ideal imaging modality. Its primary merit over other modalities includes the capacity to illustrate alternative diagnoses contributing to the symptoms. CT is definitive in the majority of the instances and has higher diagnostic accuracy. Old CTPA protocols have a mean effective dose of 3mSv.

1.5.1.7.1: Advantages of CT Over Other Imaging Modalities

The primary merit of CT is that it has greater diagnostic accuracy and is definitive in many instances. It is easily accessible in emergency departments and has rapid images acquisition when compared to V/Q scan. As soon as images are available, most physicians can easily recognize PE

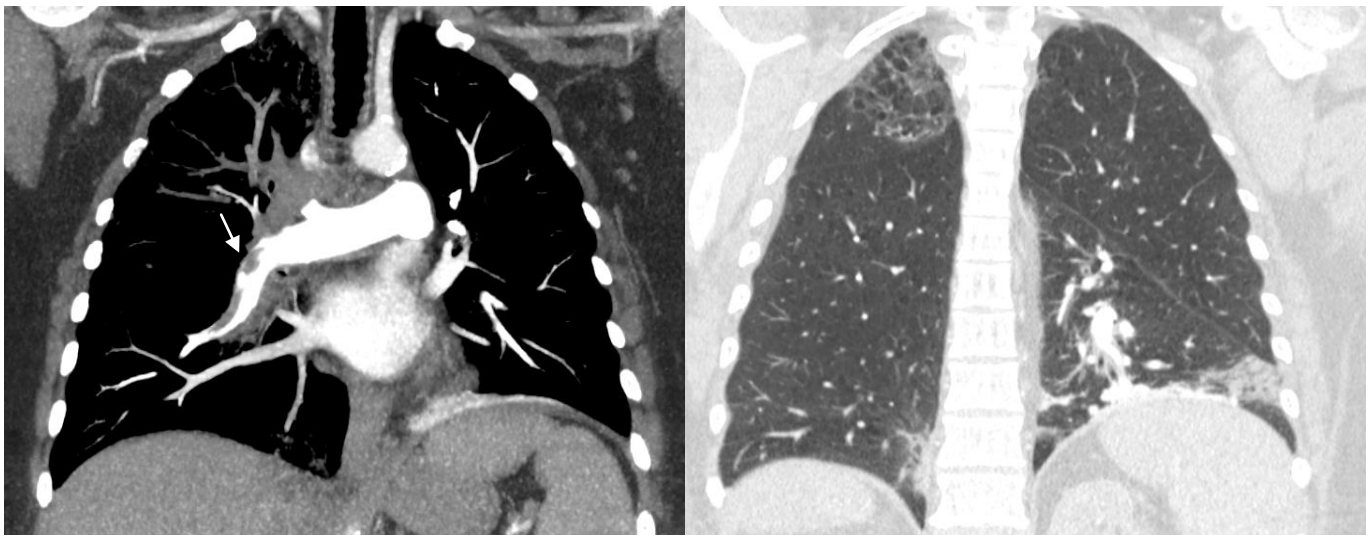
filling defects. It also has the ability to provide vital information about the mediastinum, lung parenchyma, pleural space and chest wall and can reveal other diagnoses contributing to symptoms.

1.5.1.7.2: CT Findings

CT pulmonary angiogram findings include filling-defect with the pulmonary arteries. The appearances are either central, doughnut sign, railroad track sign, rim sign or eccentric clot.

In rare cases, secondary findings are mosaic attenuation with reduced vasculature, pulmonary infarction with airspace or peripheral opacity, atelectasis, small pleural effusion, and right heart strain.

Figure 1.20(a) demonstrates PE Filling-defect within the right main pulmonary artery.



a b

Figure 1. 20: Low dose CTPA with filling defects, (a) shows major right pulmonary artery PE(arrow). (b) shows a wedgelike consolidation in the left lower lobe posteriorly, and COPD changes are demonstrated in the upper lobes.

1.5.1.7.3: CT Limitations

The main limitation of CTPA includes a high number of suboptimal or non-diagnostic examinations because of low-contrast enhancement, motion artefact, restricted venous access, low or sluggish contrast flow to peripheral pulmonary arteries, an incorrectly placed region of interest (ROI) triggering the scan, Valsalva from improper breathing technique, or insufficient cannulation flow rate. Many of these patients may require repeat examinations or VQ scans; thus, this radiation exposure was unnecessary.

1.5.1.7.4: Definition of Radiation Dose

When patients undergo CTPA, they are required to go through a scanner and receive a radiation dose that varies with respect to scanning factors used and body size. To describe radiation doses, two

common measurements used are dose length product and effective dose. The dose length product or DLP is the length of the scan multiplied by the CT dose index (CTDI); the latter expresses the exposure of radiation expressed in mGy, DLP is presented as mGy*cm[99]. The effective dose is the amount of radiation that is 'absorbed' based on exposure and the exposed organs or body parts; this is measured in millisieverts (abbreviated as mSv).

The effective dose of CTPA is affected by various factors such as pitch beam collimation, exposure time, and kV. The calculation is as follows:

- DLP = scan length (cm) × CTDI (mGy)
- Effective dose = k factor (0.014 mSv/(mGy*cm)) × DLP (mGy*cm)

The possibility of developing malignancy, particularly from radiation exposure, relies on organ sensitivity to radiation dose and how high the effective dose is utilised. For example, in my cancer risk calculation, it was 0.03% in one CTPA, equivalent to 1 in 2894 solid cancer cases. Nonetheless, cancer mortality is higher among young patients since their life expectancy is greater compared to the older population. Therefore, this research project aims to decrease the sum of the patient's absorbed dose while maintaining a critical imaging quality for a correct diagnosis.

The following section will discuss the CT image quality check required prior to the low dose CTPA studies.

1.5.1.8: Image Quality Check Prior to the Study.

Image quality checks were performed before the low dose CTPA experiments to ensure that the scanner's accuracy was consistent with manufacturing specifications. The Toshiba principal engineers at the Australian Capital Territory office undertook the test [100]. Essential performance parameters checked were image noise, nominal tomographic section thickness, contrast scale, contrast resolution, the dose per scan and the final image quality. The following steps were taken during the image quality check.

1) Preparation for Image Quality Check.

- In the first step, if tube OLP (illustrated below) was Less than 20%, a warm-up was performed.

Figure 1. 21. Tube warm–up a warm-up was performed as OLP showed zero.

- In the second step, phantom tombstone fitted to couch, head or footrest, is removed as required.

Figure 1. 22. Phantom Tombstone fitted to the couch.

- In the third step, Toshiba phantom on tombstone mounted.

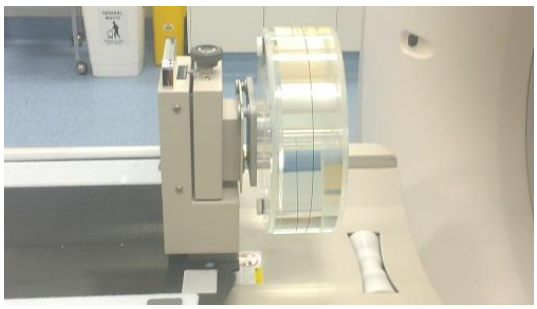


Figure 1. 23. Toshiba Phantom on Tombstone mounted at headrest position.

- In the fourth step, outer lasers are used to align in both Vertical and Horizontal planes.

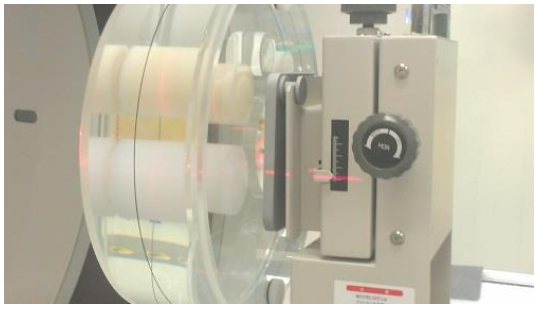


Figure 1. 24. Outer lasers are utilised to align the planes.

- In the fifth step, the phantom is centred using the Zero button on the panel

Figure 1. 25. Arrow showing phantom is centred using the zero button on the panel.

Select Exam Plan

a) Patient details are entered as Toshiba IQC

b) Toshiba Image Quality Exam Plan is selected under Protocol Group C.

c) Conditions are confirmed as

   i) 120kV, 300mA, Rotation Speed 1 sec, 4mm x 4, Slice thickness 8 mm Filter FC70

   ii) Exposure of phantom Performed.

2) Measurement of Results

a) The first image was selected, then the measurement tool was selected, circular measurement tool was selected and reduced to 25 x 25 ROI.

b) ROI was copied five times to give us a total of six ROI.

c) ROI was placed over measurement points, air, Delrin, acrylic, nylon, polypropylene and water, as illustrated below figure.

d) Results are recorded on the Image Quality Check Sheet and compared to the expected attenuation coefficient of each test.

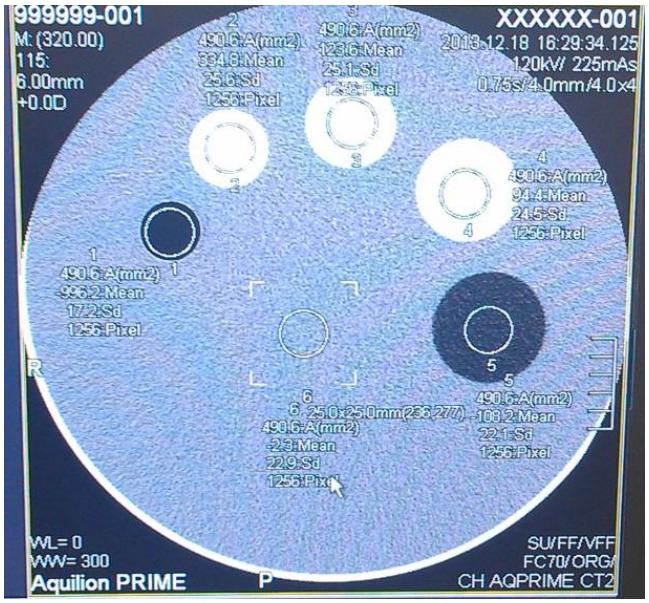


Figure 1. 26. The phantom test provided the anticipated attenuation coefficient of each test.

The final image quality was validated by the Toshiba principal engineers and demonstrated consistency with manufacturers' specifications[100].

In summary, in chapter one, it was found that PE diagnosis is always challenging because its symptoms are non-specific and similar symptoms may be found in many other cardiac and acute respiratory ailments. Hence, probability testing and D-dimer testing should be conducted to identify if further imaging is required after undertaking a history and physical examination. A chest x-ray is the initial imaging in patients with suspected PE to exclude an alternative diagnosis, primarily acute respiratory illness, for example, pneumonia or pneumothorax

Chapter 2: Literature Review

2.1: Section One: Current Literature of Low dose CTPA Protocols

2.1.1: Aim

The purpose of this chapter was to establish familiarity and understanding of the current literature review on low dose CT pulmonary angiogram and solutions for suboptimal CTPA examinations. This chapter will have analysis of relevant publications on low dose CTPA and suboptimal CTPA examinations

2.1.2: Introduction

Computed Tomography Pulmonary Angiogram (CTPA) remains the contemporary gold standard for imaging pulmonary embolism in suspected patients. However, a major drawback of the standard CTPA examination is high radiation exposure, a lower mean effective dose ranging between 3- 5mSv. [18, 101, 102]; the mean effective dose could reach 15mSv [16, 18].

The established diagnostic reference level (DRL) of CTPA from Switzerland, Saudi Arabia, Netherlands, Malaysia and the United Kingdom range from 4.6 mSv to 6.5mSv[14, 103-106]. In Ireland, the mean effective dose of CT pulmonary angiogram was 324 across 34 CT scanners surveyed, which is a little lower than the diagnostic reference level established in the below four countries[14, 104, 105, 107, 108].

Table 2. 1: Comparison diagnostic reference level in DLP(mGy cm).

467	440	480	350
Switzerland (2010)	UK(2019)	Saudi Arabia (2014)	Netherlands (2012)

Reliable studies ascertain a considerable linkage between radiation exposure and cancer risk, although it is difficult to quantify the effects of CT examination on cancer rate. However, CT is estimated to contribute an estimate of 2 % of the case of cancer [109]. About 15 to 30 cancer-related deaths per a hundred thousand are anticipated in patients having the examinations with an effective radiation dose ranging from 3 to 6 mSv [110]. Recent studies reveal that cancer risk during their lifetime is even much higher in younger patients undergoing CTPA[111, 112]. CTPA delivers a higher effective dose to breast tissue; the radiation dose was 2.5-5.3 times higher than V/Q scan, although lung dose is 2.4-4.6 times higher for V/Q scan[113]. The reported breast radiation dose by the European Society of the cardiologist

was between 10 to 70mGy, this much higher than that of the perfusion scan, which was 0.28-0.50 mGy[79]. The risk of breast cancer due to CTPA is even higher, given the breast tissues high radio-sensitivity[114, 115]. Hence there is a need to utilise the lowest possible radiation dose[116]. Various dose reduction strategies have been implemented so far. Apart from tube current modulation, noise filters and high CT pitch and iterative reconstruction, radiation dose savings could be achieved by a reduction in either kV or mAs [117-119].

This review will explore the current literature of low dose CTPA protocols focusing on mainly low tube voltage protocols and other emerging low dose techniques. Low tube voltage techniques have been recommended and considered an optimal method to reduce radiation dose in patients by multiple recent studies[120-124]. However, the 80kV technique is not utilised in Australia due to increased image noise and expectations of high-quality CT images. Therefore this review seeks to examine the existing literature on the methods to reduce radiation dose and image noise whilst simultaneously maintaining the diagnostic accuracy of CTPA. Additionally, this literature review seeks to provide a report on the strengths as well as limitations of current low dose techniques utilised in the evaluation for PE suspected patients. The information obtained from the systematic review will provide a basis to improve the anticipated low dose CTPA protocol.

2.1.3: Search Strategy

Several databases were utilised to provide broad coverage of the current medical literature relating to low dose CTPA protocols and CTPA in general. The databases that were searched were: Science Direct, Google Scholar, Medline, Scopus and CINAHL.

The search strategy involved a combination of the term, for example, 80kV "OR" CTPA "OR" CT pulmonary angiogram "OR" Pulmonary angiography "OR" effective dose "OR" dose length product "OR" low kilovoltage "OR" image quality "OR" imaging pregnant patients. An "AND" additional method used was also used in terminology when applicable, for example, 80kV "AND/OR" CTPA "AND/OR" CT pulmonary angiogram, alternatively low dose CTPA "AND" low kilovoltage "OR" image quality "OR" imaging pregnant patients. The search terminologies are listed in table 2.2.

The search was limited to literature from 1990 to the present (2020). The rationale for this strategy is that CTPA was invented in the mid-1990s.

2.1.4: Article Selections Process

Initial screening of the literature included perusal of article's title, authors, affiliation-academic institute, and publisher to determine articles' relevance. Of the remaining articles, the secondary assessment was conducted; this further evaluated if the abstract information was applicable to this

literature review topic, if it was current or recent, the quality of the article and its scholarly journal were also evaluated. Tertiary assessment of the articles' content was conducted to ensure that they were peer-reviewed, whether a systemic layout with abstract, introduction, methods, discussion, conclusion and in-text citations and a full list of references indicating sources authors used to back up their research and whether there was logical flow from research to discussion and conclusion.

The most comprehensive assessment was the tertiary assessment. This considered whether the method's description allows other researchers to replicate the study, whether authors fully explained sampling techniques, size, and eligibility of the participants and/or concern for reliability, the validity biases. When checking the strength and shortcomings of the article, questions asked include whether the research question and objective are clearly defined. Is the study design appropriate for the posted research question, is the sample size, data collection, and statistical measurement appropriate. Are the study question and objectives answered?

As described in PRISMA review, the review guideline required assessing if results are statistically analysed, whether the test method used is appropriate and if the graphs and tables used to present results promote the text's clarity[125]. Furthermore, in each article's discussion, this review checked how findings are interpreted to show insight or explain what findings mean to readers whilst comparing with previous studies. Finally, this review checked if the conclusion clearly restates the existing literature's major findings and contribution. Articles with unclear methods or with missing data were excluded from the review. Only scholarly articles related to the research question added understanding of the research topic and fulfilled the above criteria were deemed a good source for this literature review.

The inclusion criteria were set:

- Population (male, female, human)
- Age (adult >18 yo)
- Language (English)
- Publication year (2000-2020)
- The accessibility of the full article contents

2.1.5: Results

The database searches identified 1546 publications, including 178 from Medline, 765 from Science Direct, 245 from Google Scholar, 205 from Scopus, and 153 from CINAHL. The search strategy for Google Scholar required modification was many less relevant results were identified.

On review of the studies, 182 duplicates of studies were excluded after the initial screening on the title, and abstract 1271 articles were excluded after being identified as less relevant to the research topic, case report or editorials.

After this process, 93 articles were considered for secondary review, where 49 studies were excluded after being identified as of lesser quality or missing data as per the above search strategy criteria.

For the final review, 44 studies were retained as they were relevant, up-to-date, and of sufficient scholarly quality with detailed information on methods and data analysis. Although many of the studies published within the last decade were included to take into account advances in CT technology, high quality older studies from the well-trusted authors were also considered. The database search process is visually presented in figure 2.1.

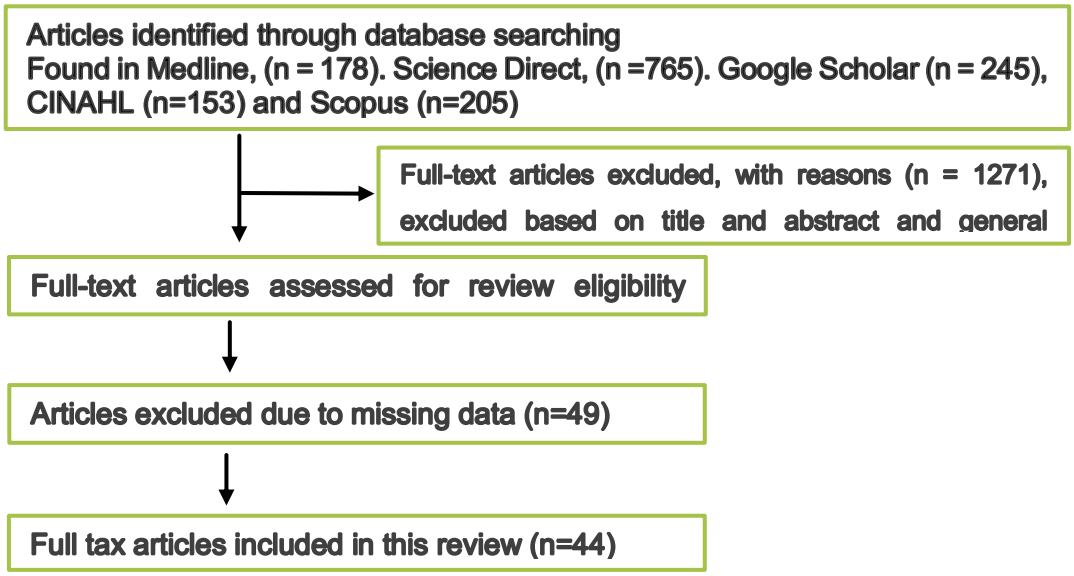


Figure 2.1: Database searches process flow diagram.

Table 2.2: Search strategy and the term used to find the relevant studies.

Intervention	Group	Additional search
Low dose Low dose computed tomography 80kV Radiation dose Breast dose Pitch mAs Reconstruction Algorithms Tube current Standard deviation Pulmonary embolism, PE Suboptimal Non-diagnostic	CTPA CT pulmonary angiography CT pulmonary angiogram Computed tomography dose index Effective dose Dose length Product Pulmonary embolism Low kilovoltage Pregnant patients Image Quality	Emergency department Pulmonary imaging Radiology imaging

This review included studies undertaken in diverse countries globally, including countries in Europe, USA, Australia and Asia. The selected studies were organised into subsections to address a different aspect of the research topic.

This literature review was addressed using a thematic approach. This study's purpose is different from many approaches to low dose CTPA conducted over many years. Therefore this review is organised into subsections to address the key areas of interest in the research topic, for example, tube voltage, tube current, image noise, CT pitch value, algorithms, image noise reduction techniques, tube current standard deviation and review on emerging technologies such as dual CT scanning

techniques. This literature review also looked into studies that assessed the non-diagnostic rate of CTPA. The literature review concept has been explained by the following authors[125, 126].

The main concept of the studies, study titles, aims, main findings are summarised in table 2.3.

Table 2. 3: Main findings and summary of the relevant literature review.

Tile	Aim	Findings	Comments
Low-dose pulmonary CT angiography reduced radiation exposure and iodine load at low tube kilovoltage [18]	Explore the potential benefits of reduced tube voltage in decreasing radiation exposure.	This study shows that 80kV allows a substantial reduction of radiation dose. For instance, the tube voltage reduction from 120 to 100 and 80 kV reduce dose by 41 and 74%, respectively. Estimated effective dose was 3.38mSv in 120kV and 0.9mSv in low dose. However, increased image noise severely affected the mediastinum patients weighing above 75 kg. Using low tube current, decreases contrast to noise ratio compared with normal radiation exposure. This is a result of the iodine signal, which remains constant at an increased image noise level when using low mAs[18] .	Image noise is the main limitation reported; the author indicates image noise reduction techniques may play a significant role in the wider distribution and acceptance of the 80kV protocol. It can be reduced by using wider CT window settings, Increasing reconstruction thickness, and using soft kernels for image reconstruction. This technique has not yet widely implemented. **Comments** The author suggested soft kernels for image reconstruction. The author acknowledged the need for a comprehensive scientific examination before the routine implementation of this protocol.
Detection of pulmonary emboli with CT angiography at reduced radiation exposure and contrast material volume: comparison of 80 kVp and 120 kVp protocols in a matched cohort	This study aimed to explore the possibility of detecting PE with reduced radiation exposure of CT angiography.	All patients with pulmonary embolism were correctly identified with both protocols. Overall subjective image quality was higher at 120 kV compared with 80 kVp.[24]	This study evaluated the detection rate of pulmonary emboli CTPA using either a standard 120kV or an 80kv low-dose protocol. High kV produced better image quality, but with higher radiation dose[24]
CT Pulmonary Angiography at Reduced Radiation Exposure and Contrast Material Volume Using Iterative Model Reconstruction and iDose[4] Technique in Comparison to FBP[26]	This study aimed to evaluate the image quality of CTPA at reduced radiation dose using two different reconstruction, iterative model reconstructions(iDose4 and IMR) compared to filtered back projection	In this study, a noise reduction of 55% was attained with iDose4 and 85% with IMR compared to filtered back projection. contrast-to-noise ratio noticeably increased with iDose4 and IMR compared to filtered back projection [26]	Subjective and objective image quality and accuracy in detecting of PE were assessed In statistical analysis, authors indicate a qualitative Likert scale model; however, there is no clear explanation of the method's consistency and accuracy.

Tile	Aim	Findings	Comments
Ultra-low dose contrast CT pulmonary angiography in oncology patients using a high-pitch helical dual-source technology	The objective of this study was to examine if the image quality and vascular enhancement are preserved in CTPA studies performed with ultra-low contrast and enhanced radiation dose using high pitch helical[127].	The image quality of protocol was excellent, a low dose of iodinated contrast media and radiation dose is achieved using a high-pitch helical acquisition mode in a dual-source scanner[127]	The scanner used was a 128-slice dual-source scanner, with a high pitch helical 3, which was different from normal single-source scanners. Radiation dose is reduced, the average radiation dose length product (DLP) was 161±60 mGy.cm. Note oncology patients are different than the general population.
80-kV Pulmonary CT Angiography With 40 mL of Iodinated Contrast Material in Lean Patients[128]	This article aims to compare the vascular enhancement obtained with 80kV CTPA protocol in lean patients[128].	This study shows that 80kV can achieve excellent image quality in lean patients; in this study, pulmonary arteries enhancement increases down to the subsegmental level[128].	**Comments** This study was conducted in the diagnostic and Interventional Radiology, the University of Pisa, Italy by Faggioni et al. shows using a tube voltage of 80 kV results in a radiation exposure saving of 2.8 times compared with 120 kV, due to the lower x-ray energy. The overall study seems to reliable and acceptable.
Reducing computed tomography radiation dose in diagnosing pulmonary embolism[129]	This study aimed to optimise radiation dose while maintaining image quality to ensure minimum radiation dose. Five extra seconds were added before starting the scan for bolus tracking, as the contrast medium could not have reached the pulmonary artery in the first 5 sec[129].	In this study, the average effective dose was significantly higher in the first group 5.4mSv compared to the second group 3.3mSv [129]	Comments Radiation is still high at 3.3mSv. You can also have problems with tachycardia and pregnant patients who require a short delay time.
Double-Low Dose Protocol of CTPA in the PE: A Feasible Approach for Reduction of Both Contrast Medium and Radiation Doses[130]	The aim of this article was to evaluate the strength of double low-dose protocol of CTPA in the diagnosis of pulmonary embolism[130]	This study shows that lower dose protocol leads to a significant reduction in radiation exposure and contrast medium dose when compared to the high-pitch spiral dual-source CT pulmonary angiography[130].	Comments This study seems to be reliable and of high quality. However, our radiologist is reluctant to use high pitch due to fear of missing PE in subsegmental level.

Tile	Aim	Findings	Comments
Evaluation of image quality and radiation dose reduction comparing knowledge model-based iterative reconstruction on 80-kV CTPAwith hybrid iterative reconstruction on 100-kV CT[123]	This study aimed to assess dose reduction and image quality of low tube voltage 80kV CTPA protocol using iterative reconstruction (IMR) and compared with 100-kV CTPA with hybrid iterative reconstruction[123]	low-kV IMR-CTPA presented lower DLP (248.24 vs 352.4mGy × cm) of the 100kV	Comments. Lower DLP of 248.24 is considered to be high.
Reduced-Dose Low-Voltage CTPA with Sinogram-affirmed Iterative Reconstruction versus Standard-Dose Filtered Back Projection[22]	This study aimed to assess the image quality of low-voltage CTPA with raw data–based iterative reconstruction in comparison with the image quality of standard-dose standard-voltage[22]	This study shows that iterative reconstruction yielded equivalent the image quality of low-voltage half-dose CT angiograms compared with standard-dose FBP CT. Mean effective dose of the low dose was 1.31mSv. On the image quality assessment, 80kV was reported to have increased image noise [22]	Comments On 80kV images, subjective image noise increased with increased patient weight significant. That resulted in only a proportion of examinations rated as having good image quality (score 2), which means having increased image noise but diagnostic quality.
An optimized test bolus for computed tomography pulmonary angiography and its application at 80 kV with 10 ml contrast agent[131]	This study aimed to decrease radiation dose and contrast by using personalised for CTPA examinations at 80 kVp with 10 ml contrast agent to reduce iodinate load and optimise radiation dose.	This study shows the possibility of having personalised protocol could be used for CTPA examinations at 80 kVp with 10 ml contrast agent to obtain sufficient image quality with a low iodinate load.	Comments This study cannot be replicated by just reading the manuscript; it seems vital details are missing. For example, and, e.g. how significant is missing diagnosis in peripheral pulmonary arteries with low contrast volume.
High pitch computed tomography pulmonary angiogram with iterative reconstruction at 80kV and 20 mL contrast agent volume[132]	This study intended to evaluate the image quality, radiation dose and diagnostic accuracy of 80kVp, high-pitch CTPA with iterative reconstruction using 20 ml of contrast agent.	**Method**: n = 50 each; group A, 100 kVp, 1.2 pitch, 60 ml of contrast medium and filtered back-projection algorithm; group B, 80 kVp, 2.2 pitch iterative reconstruction with 20 ml of contrast medium.	Comments There was no significant difference in diagnostic accuracy between the two groups. The dose of the low dose was 1mSv. The study was undertaken at Jinling Hospital, Medical School. Patient size may be smaller than the Australian population.
Low radiation and low-contrast dose CTPA Comparison of 80 kVp/60 ml and 100 kV/80 ml protocols[133]	This study aimed to evaluate image quality and diagnostic accuracy of low dose protocol in terms of	In the patient's ≤80 kg, CTPA protocol allows similar image quality to be achieved compared with the standard CTPA	Comment Clinical Universidad de Navarra publishes the article, Pamplona, Spain, data seems to be

Tile	Aim	Findings	Comments
	radiation and contrast volume saving.	protocol while reducing radiation exposure by 60% and contrast media volume by 25%.	acceptable overall with minor limitations
Investigating the use and optimization of low dose -kV and contrast media in CT Pulmonary angiography examination[134]	This study aimed to investigate the usefulness of 80kV CTPA for the diagnosis of pulmonary embolism.	This study shows decreasing the tube voltage increases noise while increasing the image contrast. As a result, the signal-noise ratio is reduced since the relative increase in noise is more than the increase in image contrast.	Comments Image noise increases with increasing image contrast. As a result, the signal-noise ratio is decreased. Hence there is a need for image noise reduction.
CT pulmonary angiography: simultaneous low-pitch dual-source acquisition mode with 70kVp and 40ml of contrast medium and comparison with high-pitch spiral dual-source acquisition with automated tube potential selection	This study aimed to evaluate a 70kVp CTPA protocol's feasibility using dual-source with 40ml of contrast medium and comparison with a high pitch spiral dual-source protocol[135].	This study shows acceptable image quality in patients with a BMI of up to 35 kgm22. With a reduction of radiation exposure by almost 50% and a reduction of contrast dose by 40% compared with a spiral acquisition high-pitch CTPA protocol[135].	Comments This study was undertaken University Dusseldorf, Germany; it seems accurate and reliable low-pitch dual-source acquisition mode, which we do not have access and low kV is beneficial only patients with a BMI up to 35 kgm22. [135].
Submillisievert standard-pitch CTPA with ultra-low dose contrast media comparison to standard CT imaging[136].	This study aimed to assess the image quality and radiation dose of standard-pitch CT pulmonary angiogram with ultra-low dose contrast media administration in comparison to standard CTPA[136].	80kV protocol resulted in radiation dose reduction by 71.8%. However, this protocol results in increased image noise. Therefore, we observed slightly lower signal intensity, SNR and CNR values of the pulmonary artery when compared to standard CTPA[136].	Comments Authors observed slightly lower signal intensity, SNR and CNR values, this consistent to other studies.
70 kVp computed pulmonary tomography angiography: potential for reduction of iodine load and radiation dose[120].	This study aimed to evaluate 70kV dual-source CTPA with less iodine compared to single-source 70kV and 100kV protocol[120].	Single source 70kV CTPA allows for significant radiation dose reduction with a comparable signal to noise ration and contrast to noise ratio, where compared to dual source CTPA[120].	Comments There are fewer details how single source 70kV CTPA allows a comparable signal to noise ration and contrast to noise ratio to 100kV protocol? There is less details on parameters and radiation reduction software.

Tile	Aim	Findings	Comments
The image quality of low mA CTPA reconstructed with model-based iterative reconstruction versus standard CT pulmonary angiography reconstructed with filtered back-projection: an equivalency trial[137]	This study aimed to evaluate whether CTPA using low mA setting 100 kV, 20 mA is equivalent to routine CTPA at 100 kV, 250 mA reconstructed with filtered back-projection [137].	Low mA CTPA is equivalent to routine FBP-CTPA and allows a significant dose reduction while improving SNR and CNR in the pulmonary vessels, as compared with routine FBP-CTPA[137].	Comments artefacts in the shoulder region are reported when using low kV and low mA, which means increased exposure or image noise reduction is required.
The image quality of low mA CT pulmonary angiography reconstructed with model-based iterative reconstruction versus standard CT pulmonary angiography reconstructed with filtered back projection: an equivalency trial[137]	The aim of this study was to determine whether CTPA using low mA setting reconstructed with model-based iterative reconstruction (MBIR) is equivalent to routine CTPA reconstructed with filtered back projection (FBP) [137].	The study used low mAs, hence the reported estimated effective doses were 0.3±0.03 vs 4.1±1.1 mSv, p<0.0001[137].	Images were non-diagnostic in patients greater than 30 kg/m2, images were graded as insufficient for diagnostic PE. 44 % were potentially non-diagnostic CTPAs in this category of patients[137].
Low dose computed tomography pulmonary angiography protocol for imaging pregnant patients: Can dose reduction be achieved without reducing image quality[138].	The aim of this study was to assess the effect of low dose CTPA on radiation dose in pregnant patients when kV is decreased from 120kV to 100kV[138]	Mean effective The low dose group dose was 0.97 mSv compared to 1.66 mSv in the 120kV group (P b 0.001) [138].	With 100 kV rather than 120 kV authors found increased noise. However, no major difference in image noise was observed. One radiologist reported better vessel opacification in low dose scans[138]
Rate of Non-diagnostic CTPA Performed for the Diagnosis of PE in Pregnant and Immediately Postpartum Patients [28].	This study aims to assess the non-diagnostic rate CTPA in pregnant and postpartum patients with suspected PE to decide whether VQ scan or CTPA should be considered best imaging [28].	Eighty-three pregnant or postpartum patients included in this study. 36 (43%) pregnant or postpartum patients attained a non-diagnostic CTPA examinations, while 24 (26.9%) non-pregnant or postpartum patient CTPAs were non-diagnostic. Given the non-diagnostic rate patients with normal chest, X-ray should use VQ can as first-line imaging [28]	Comments This study was undertaken in a Canadian hospital and shows suboptimal studies are common in pregnant and postpartum patients. However, while it is difficult to eliminate, it is possible to reduce it as discussed in this research's pregnant chapter.
The indeterminate CTPA imaging characteristics	This study aimed to evaluate the rate of	A retrospective review of 3612 CTPA, none diagnostic scans were	Comments Low contrast attenuation in the main pulmonary artery

Tile	Aim	Findings	Comments
and patient clinical outcome[30]	suboptimal and non-diagnostic CTPA[30].	six percent, the most common cause of suboptimal examinations as motion and poor contrast enhancement. Contrast attenuation in the main pulmonary artery was 245 HU +/- 80 (standard deviation) in patients.	and motion artefact was the main cause of suboptimal examinations. This consistent with other studies which reported similar findings.
Patient outcomes following suboptimal and non-diagnostic CTPA for the suspected diagnosis of PE[139]	The purpose of this study was to assess the rate of suboptimal and non-diagnostic CTPA[139].	Twenty-three percent of the CTPA examinations (369/1619) were suboptimal, and further 4%(59/1619) were non-diagnostic studies.	Comments Poor contrast enhancement was the most common cause of non-diagnostic and suboptimal studies, followed by motion artefact and body habitus. Twenty-five percent (15/59) of non-diagnostic studies were repeated, and none were positive for PE[139]. This study was published American Thoracic Society journal; it appears to be very reliable data. However, 23% seems very high maybe this study reported also suboptimal manor studies.

The review clearly indicates that Image noise is the main limitation reported; the authors indicate that image noise reduction techniques may play a significant role in the wider distribution and acceptance of the 80kV protocol. On the other hand, although suboptimal and non-diagnostic studies resulting from poor contrast enhancement are major limitations reported, few studies discuss ways to solve non-diagnostic studies. Hence further study is needed in decreasing radiation dose and non-diagnostic studies.

2.1.6: Analysis and Discussion

Various dose reduction techniques were covered in this literature review and showed substantial radiation dose saving possible through these techniques. There were techniques that this research is interested in exploring during this review; these include increasing pitch value or decreasing in either the current tube setting or the tube voltage while maintaining image noise.

2.1.7: Reducing Peak Kilovoltage

Lowering peak kilovoltage (kV) is an effective direct method of achieving a substantial radiation dose reduction; several researchers have confirmed this solution [140-144]. Reducing tube voltage from 120kv to 100kv results in greater than 30% dose reduction. Concurrently reducing the kV from 120 kV to 80 kV, radiation dose decreases 65% if all other scanning parameters remain constant[145].

Following the above publications, other researchers have reported the possibility of scan protocols with lowered tube voltage at 80 kV without significantly compromising image quality while also improved vascular enhancement [22 120, 122, 146, 147]. Other studies have investigated 80kV techniques to reduce radiation dose. Gillespie et.al[94] and Halpenny et al. [138] from the University of New York also found that 80kV lower tube voltage could produce acceptable image quality in pregnant patients suspected of PE. A constant issue in these studies was that lower kV resulted in significantly increased image noise. For example, if kV was reduced from 120 to 80 kV, some CT scanners required an almost fourfold increase in mAs to maintain constant image quality[148]. Several reliable studies have investigated the utilisation of lower tube voltage and found a significant reduction in radiation dose with a lower 80kV but also a considerable upsurge in image noise, which was generally found to reduce image quality [120, 136, 149-151]. These studies also found the general trend of increased noise, but this varied from minimum to massive and that this was dependant on the habitus. A major

issue with this approach is that many CT scanners may automatically handle the problem of image noise by raising the tube current to offer maximum image quality; consequently a limited radiation dose reduction is achieved when this approach is utilised alone[22].

Studies undertaken in imaging departments in south-east Asia revealed that 80 kV CTPA allowed diagnostic image quality among patients with a weight of up to 90 kg[146.] These findings have further been confirmed by a study conducted in the University of Pisa, Italy, by Faggioni et al., who confirmed using a tube voltage of 80kV results in a radiation dose reduction of 2.8 times compared with 120 kV, due to the lower tube voltage energy[128]. However, 80 kV increases image noise, leading to a deterioration of image quality in larger patients [128, 152]. For this reason, the above radiology department decided to restrict the analysis to lean patients with body mass index ≤ 23 kg/m^2) to keep noise within acceptable limits[128]. Even though the primary focus for imaging and quality is a pulmonary arterial system, accidental findings in the lungs, such as pneumonia, pulmonary oedema, atelectasis, and lung nodule, are common[23]. Hence, it is essential to maintain image quality and diagnostic confidence for excluding incidental findings in both the mediastinum and lungs while using the 80 kV tube voltage.

In a smaller number of patients, the diagnostic accuracy and the image quality in lung parenchyma using the 80 kV and 120 kV were comparable [23]. According to Szucs-Farkas (2010), observation suggests consolidative changes such as pneumonia or lung nodules could be confidently detected at 80kV. However, other authors suggested that even though image noise increases, increased mediastinum noise does not affect assessing the pulmonary arteries and does not hinder PE exclusion. When explicitly assessing for only lungs and mediastinal disease, imaging departments utilize the routine CT chest protocols with a higher tube voltage of 120 kV[18].

Several studies have speculated or theorised a possible increase in image noise at the 80 kV protocol severely affecting both mediastinal and lungs assessment, especially in patients with weights greater than 75 kg; this is supported by several authors who have investigated image quality[18],[128, 152].

Therefore, the vital question that would require a detailed answer in a low dose CTPA protocol would be: How can image noise be reduced whilst maintaining a low dose?

2.1.8: Increasing Helical Pitch

Helical CT pitch is a measure of the table speed; it is described by formula $Pitch = \frac{F\ table}{nT}$, where F table denotes the table feed distance for each 360-gantry rotation and nT denotes collimation beamwidth [135, 136]. The general relationship between pitch and dose is that the patient's radiation dose decreases when the pitch increases. The reason for dose reduction is that if the pitch value of less than 1 (indicated slower scanning), then the scan irradiates the same area multiple times therefore overlapping. However, if the pitch value is higher than 1, then the radiation dose decreases from less overlap; this has been confirmed by several researchers [132, 135, 153-155].

Increasing in the helical pitch minimizes the radiation dose proportionally except for some scanner that automatically increases tube current with increased helical pitch; this results in limited radiation dose saving. Also, an increase in the helical pitch, in some instances, reduce z-axis resolution[156]

An important issue stated by some studies is that using high pitch without reducing kV or mAs does not lead to the desired radiation dose reduction; the reported average effective dose was higher than 3mSv[157, 158]. Rajiah et al. (2019) stated that using a helical high-pitch acquisition technique could provide good image quality with accurate visualization of peripheral segmental/sub-segmental branches with an effective dose of 2.25mSv. The benefits still include utilising a small volume of IV contrast agents, less patient motion, and faster scanning time[127], this issue, however, is that radiation dose is still substantial for contemporary standards and in important subgroups such as pregnant and young patients.

Another potential issue is high pitch, fear of missing small PE, and acceptable Australian standards for image quality and regulations are higher; hence, the radiologists in this imaging department would disagree with high pitch value.

2.1.9: Reducing Tube Current

Decreasing mAs is another method to reduce radiation dose. The results of several studies indicate that mAs may be lowered from 200 mAs to 110-140 mAs without visually affecting the image quality[19, 148, 159]. Some groups have even achieved reducing tube current to 50 or 44 mAs[17 18]. However, using low tube current in CT pulmonary angiogram decreases contrast to noise ratio (CNR) compared with normal radiation exposure. This is the result of the iodine signal, which remains constant at an increased image noise level when using low mAs [18, 19]. Some research suggested using a fixed tube current; however, a fixed tube current

has the disadvantage of inaccurate exposure for variable patient sizes[137]. For example, suppose the imaging department uses fixed lower mAs radiation exposure among patients with large body habitus. In that case, imaged quality could be affected, resulting in a higher number of non-diagnostic scans. The converse situation is that when a fixed mAs is used among small-sized patients, radiation exposure may be much higher than necessary, causing an unrequired radiation dose that has not contributed benefit to the patient[18]. This technique's overall weaknesses are the inability to offer a precise exposure for variable patient sizes unless an exposure chart is used, and the exposure chart is impractical for a busy imaging department.

The best solution for dose reduction with tube current reduction is using tube current modulation; this safeguards the quality of the image in all patient sizes. Tube current modulation is a technique for adjusting the tube current to follow the changing patient anatomy obtained via the scanogram. Modulating tube current was discovered to deliver a considerable dose of decrease of up to 40%; thus, it should be used in this low dose protocol[160]. The major advantage of tube current modulation is providing appropriate tube current method settings for patients with variable sizes and excellent image quality[148]. Overall, less research was conducted on the diagnostic image quality of low mAs CT pulmonary angiogram than lower tube voltage.

Using lead protection outside the field of view and bismuth breast shield are other techniques used to reduce radiation dose further. Bismuth breast shield minimises the radiation dose. However, increased image noise and streak artefact has been reported as the main limitation of this technique[161, 162].

2.1.10: Image Noise

The number of x-ray photons detected per pixel is also referred to as the signal to noise ratio (SNR)[163]. CTPA image noise is identified by calculating the size of random Houndsfield unit (HU) fluctuations within a defined region of interest, which is expressed as standard deviations (SD). Signal-to-noise ratio (SNR) may be enhanced by increasing the radiation dose or noise reduction techniques[164]. CT scanning parameters, including the tube voltage, helical pith, scan speed, tube current geometric detector efficiency, slice thickness, patient size, and scanner efficacy, influence image noise in CTPA examinations. The amount of the x-ray photons that reach the patient is dictated by the CT scanning parameters as above. Similarly, the number of x-ray photons leaving the patient's body that is converted into image signals is determined by the scanner efficiency[165]. As different scanning parameters

have different trade-offs, hence image noise can be combated effectively with just an understanding of the trade-offs. Considering this, a study suggested the following noise-reducing strategies as the methods to manage increased noise arising from a low kV CTPA.

First, doubling the reconstruction thickness of the CTPA images as low as 0.625 to 1.25 is the first method to limit image noise; this technique reduces the image noise by 30% since the image noise is proportional to the square root of reconstruction thickness[166]. The increase in the reconstruction thickness reduces image noise proportionally. However, the increase in slice thickness has some significant consequences, such as the decrease in spatial resolution in the z-axis, which, to a certain extent, may sacrifice assessment for PE in far peripheral sub-segmental arteries. A reconstruction thickness of about 5 to 10 mm is suitable as it offers good delineation of PE with minimal noise[166]. Nevertheless, it is critical to note that this reconstruction should often be utilized alongside the original images to minimise small missing PE since this can easily be missed[23].

Secondly, the use of wider windows settings, such as the width of 750 – 900 HU and centre of 80 – 200 HU. These settings would help prevent the misdetection of tiny or partial filling effects and reduce noise perception by reducing over-enhancement in areas such as the superior vena cava[167]. Wider window settings are also the most effective strategy in lowering the streak or flow artefacts that frequently appear in the pulmonary arteries [23].

Thirdly, the use of soft kernels for reconstructing the imaging to reduce image noise. This technique effectively reduces the image noise at the expense of diminished spatial revolution and, therefore, image sharpness[168]. Therefore the author indicates that this method should not be used regularly[168]. Nonetheless, many new noise filters and reconstruction algorithms have come into clinical use as critical tools for minimizing the noise; the implementation of these techniques is widely emerging.

Notably, with all the noise reduction strategies discussed above, increasing the tube voltage or the tube current still emerges as the best and the optimal technique to minimize image noise but at the expense of accelerated radiation exposure to patients [23]. However, reducing the tube current causes a significant increase in the image noise; for example, reducing the tube current by half has an expected increase of image noise by $\sqrt{2}$ =1.414 (40%)[156]. Furthermore, reducing the lower tube voltage decreases radiation and increases the signal to contrast ratio as photon energy nears the iodine K-edge (33.3 keV), with the potential drawback of the 80kV technique causing a significant increase in beam hardening artefact and image noise[156].

2.1.10.1: Other Techniques

Other methods have been investigated to minimize radiation and image noise; these are briefly discussed below.

The dual-source acquisition is an appealing imaging technique for radiation dose reduction while, at the same time, maintaining the accuracy of diagnostics. The University of Dusseldorf study has sought to evaluate the 70-kV CTPA protocol's workability using a dual-source acquisition technique simultaneously with 40 ml contrast (less than the standard CTPA protocol). The research group carried out this evaluation amongst two large groups. Group A had a dual-source CTPA protocol at 70 kV, low pitch and 40 ml contrast with automated tube current modulation on a Siemens Healthcare CT scanner. Group B underwent the standard CTPA for the centre, which was the standard pitch, either 100 kV,120 kV or 80kVp depending on weight and 70 ml contrast. The radiation dose was decreased by 48 % in Group A compared to Group B. Further analysis showed that group A achieved comparable contrast to noise ratio (CNR) and a signal to noise ratio (SNR). The advantage was that contrast media and radiation dose were minimized in Group A. The authors concluded that radiation dose reduction could be achieved only in the event that tube current does not counterbalance radiation reduction due to lower tube voltage[135].

Similarly, Wichmann et al.'s study used a dual acquisition source with 70 kV compared with the standard 100kVp protocol. The author remarked that there were good image quality and comparable diagnostic confidences at 70 kV in the report. Nevertheless, their research has notable limitations with important data such as the bodyweight mass index not considered.

Many authors in the field consider the dual-source acquisition technique a better radiation reduction method than the single-source CT scanners; however, most radiology departments in Australia currently do not use this type of scanner.

This review will highlight two key issues in this analysis: Firstly, it is not clarified whether the CT scanners using the lower tube currents (44 mAs) or voltage (70kV) possess any superior noise minimizing software capable of further decreasing radiation exposure. For example, this imaging centre has a scanner in this department with an option to purchase Forward Projected Model-Based Interactive reconstruction Solutions (FIRST), which is a radiation reduction; however, the software costs in the vicinity of $300000. The software can decrease image noise and radiation dose at the cost of also removing critical diagnostic

information. The software was under review by the Therapeutics Goods Administration during the period of this study, and for that reason, it is not approved by the reporting radiologists.

Secondly, in relation to patients' size, many studies in Asian countries reported acceptable diagnostics accuracy in 80 kV protocol. The major issue is that the patient dimensions of the Asian population might be smaller than those of other countries, making it easier to achieve high-quality work.

Thirdly, in Australia, radiologists may prefer a high definition examination to minimize missing crucial diagnostic information and possible complaints and lawsuits resulting from poor image quality. For that reason, low tube voltage 80 kV may be less frequently used in Australia. Image noise is the likely main reason why most radiology departments continue using 100kV/120kV, and there are no credible studies available in this area from the Australian radiology departments.

2.1.11: Summary

This literature review provided background knowledge about establishing CTPA research topics and demonstrated research approaches of those who have conducted studies in this area. While there have been numerous radiation reduction techniques, including high pitch value, using Iterative reconstruction, decreasing mAs or using dual-source scanners, 80kV has been demonstrated to most significantly reduce radiation dose. The conclusions drawn from the 80kV protocol provide substantial radiation reduction and greater vascular enhancement, improving the contrast to noise ratio. However, increased image noise remains a significant limitation of the 80kV protocol. The reported increased image noise varied from minimal in small patients to very substantial in larger patients; therefore, it was dependant on body mass index.

The gap in research with regards to the low tube voltage CTPA is that most imaging departments cannot maintain image quality. Thus, new studies are needed to evaluate techniques to decrease tube voltage radiation dose and retain the image's quality without increasing tube current. This part of the review is concise because there are no current studies that adjusted the four most important imaging parameters at the same time, notably: 80kv with tube current modulation, adjusted standard deviation level, algorithm, and image reconstructions process.

The following methods will be investigated: Using improved low tube voltage 80kV protocol with an adjusted standard deviation of tube current and enhanced algorithm-kernel to enhance image quality. Image noise minimization may be achievable by using an

enhanced algorithm kernel and a slight rise in the tube current, and this can be achieved by decreasing the standard deviation of the tube current. SD can be used as a marker for the level of acceptable noise.

2.2: Section Two: The Causes for Most Suboptimal CTPA Examinations

One of the major limitations of the standard CTPA protocols (100kV and 120kV) is the high number of suboptimal or non-diagnostic studies which require repeat examinations or VQ scans.

Timing of contrast bolus, low contrast enhancement, respiratory motion and multifactorial causes are the main cause of suboptimal examinations[29]. A retrospective study of the 3612 CT pulmonary angiogram examination revealed a 6% rate of indeterminate studies; body habitus and Valsalva were listed as the main reasons for the poor image quality[30]. Likewise, another study recorded 23% (369/1619) of CTPA were suboptimal studies, and 4% (59/1619) non-diagnostic studies[169]. Low contrast enhancement was the most common reason for suboptimal and non-diagnostic studies (64% and 80%, respectively); respiratory motion and body habitus were the other major reasons causing suboptimal examinations[139].

In pregnant patients, non-diagnostic exams are even higher due to physiological tachycardia, causing reduced ventricular contrast filling with each cardiac cycle and lower contrast density in the pulmonary truck[170]. This issue caused recurrent non-diagnostic studies with pregnant patients ranging from 12% to 36%, as reported in several studies [28, 30]. A study undertaken in Canada in pregnant and postpartum women showed an even higher suboptimal examination rate of 43%, also due to mainly low contrast enhancement or Valsalva [28].

Low contrast enhancement is the leading cause of suboptimal examinations, and two solutions were suggested:

The first solution is to perform the scan at the end of expiration; this method may improve pulmonary artery enhancement[171, 172]. However, the end of expiration scans produces low image quality in lung windows, impacting diagnosing lung parenchyma diseases[171, 172].

The second solution is to use a fixed delay time of 19 seconds; this provided the optimal contrast enhancement in one study[169]. Although a fixed scan delay time is practical and straightforward to use, it is not suitable when accurate timing is required in patients with a fast heart rate, young patients, or heart failure[169].

Hence, there should be other solutions, and this study aims to explore alternative ways to reduce suboptimal examinations in PE suspected patients.

2.2.1: Summary

CT pulmonary angiogram studies revealed a large number of indeterminate CTPA examinations; low contrast enhancement, body habitus and Valsalva were listed as the main reasons for the poor image quality.

Therefore, new research is needed to decrease radiation, image noise, and suboptimal examinations simultaneously. Thus, this study will explore alternative ways to reduce radiation dose and suboptimal studies without impacting image quality. The purpose of this study is to reduce the occurrence of suboptimal image quality while improving contrast enhancement among patients investigated with CT Pulmonary Angiography (CTPA) for suspected Pulmonary Emboli (PE) by utilising an increased injection rate, lowering tube voltage (80kV) and gentle breath-holding with an open mouth.

The following chapters will discuss methods and studies undertaken to develop a low dose CT pulmonary angiogram, which is expected to reduce radiation and suboptimal examinations.

Chapter 3: Thesis Methodology

The purpose of this chapter is to describe the details of the method that is suited to answer problem statements and research questions. The findings of the study methods are discussed in either chapter 4, 5 or 6. Cross-referencing are provided at the end of each method to allow us to link other chapters which contain results and analysis of that study

3.1: Research Aim

The primary aim of this study is to reduce radiation exposure of CT pulmonary angiogram (CTPA) examinations without compromising the image quality in patients weighing less than 105kg.

3.2: Objectives

The optimal strategy to decrease radiation exposure for patients undergoing CTPA is to reduce radiation dose with each examination, reduce non-diagnostic exams and consequent re-exposure, and decrease the number of unnecessary CTPA referrals.

This study's primary objective is to design a new low-dose improved 80kV CTPA protocol with reduced image noise, which decreases radiation dose without compromising the image quality. To achieve the above objectives, this study will explore the following methods to reduce radiation dose: 1) Using low tube voltage of 80kV with tube current modulation; 2) Using an adjusted standard deviation of tube current; 3) Altering the reconstruction processing and algorithm-kernel to enhance image quality.

The secondary objective is to reduce suboptimal examinations whilst performing improved 80kV CTPA. This is attained by instructing patients to do a gentle breath-hold with their mouth open while using a high injection rate (5ml/sec) and low tube voltage. The theory behind this is to resolve Valsalva and improve contrast enhancement within the pulmonary arteries.

3.3: Research Question

How can we reduce radiation dose and maintain diagnostic confidence in detecting pulmonary embolism using the improved 80kV CTPA protocol compared to the standard 100kV CTPA protocol in patients weighing less than 105kg?

3.4: Thesis Hypothesis

H0:1) The mean radiation dose of the improved 80kV CTPA is lower than the mean radiation exposure of the 100kV protocol and still provides diagnostic confidence equal to that of the 100kV standard protocol.

H0:1.1) Improved 80kV CTPA with gentle breath-hold and open mouth allows excellent contrast enhancement of the pulmonary arteries and a lower percentage of suboptimal examinations, yet a considerable decrease in patient radiation dose without affecting the image quality.

3.5: Study Design and Data Collection

After receiving approval from the Hospital Research Ethics Committee (approval number: 15-2017) and the Australian National University ethics committee (approval number: 2020/386), this study was performed. In order to fulfil the objectives of this study and answer the hypotheses, both qualitative and quantitative methods were used.

Quantitative methods were used to low dose CTPA protocol versus the standard protocol as well as assessing the rate of suboptimal exams. The comparative study approach was suitable because there are known variables such as dose, age, and weight; numerical data was more efficiently captured, CT hardware instruments and exposure were standardised. The results were able to analysed while using numerical statistical analyses.

On the other hand, qualitative methods were more suited to explore and provide rich, detailed information about clinician views and opinions on the differential diagnosis, exploring issues such as image quality and identifying reasons for CTPA overuse. This study utilized qualitative methods such as surveys because the variables were unknown, data collection was textually based, the method was less standardised, and findings needed to be communicated in words.

3.6: Retrospective Review and Survey:

This chapter contains three studies. Stage one study discusses retrospective review, which aims to understand better PE differential diagnosis and the problem of over-utilisation of CTPA. Stage two study discusses questionnaires to senior emergency medical doctors (registrars and consultants) to identify their opinions regarding the differential diagnosis or alternative diagnoses they consider when assessing pulmonary embolus or chest pain and dyspnoea. Stage three study discusses questionnaires to senior clinicians to identify the factors contributing to CTPA over-utilisation.

3.6.1: Stage One: Retrospective Review

3.6.1.1: Aim

The retrospective review involved reviewing patient records to gather data to better understand the problem of CTPA over-utilisation and reasons for over-ordering. This study is not enough for a thesis dissertation; however, it was essential in building a case for this thesis dissertation because observation demonstrated underlining issues such as current CTPA radiation exposure, suboptimal studies and CT overuse. This study's ultimate purpose was to understand alternative diagnoses and ensure when a low dose CTPA protocol is designed and introduced, it will also be able to identify the other/differential diagnoses.

3.6.1.2: Method

A retrospective review was undertaken by extraction of CTPA reports from the centralised Picture Archiving Communication System (PACS). A sample of 748 CTPA scans among patients with suspected PE who had CT standard pulmonary angiogram was retrospectively reviewed examined to identify: 1) alternative or differential diagnosis of pulmonary embolism; 2) the percentage of positive pulmonary embolism; 3) the number of suboptimal studies; 4) the mean effective dose when the standard protocol was utilised in this imaging department. The data was collected from the imaging department at a hospital in Canberra. A Toshiba 320-row multi-detector was used in the absence of the software for radiation reduction known as FIRST [*abbreviation*].

Reports and data were collected for all CTPA examinations between the 1st of April 2018 to 31st of March 2019 (1 year period). The search term was CT pulmonary angiogram, as it is the most common name used in this imaging department. The study excluded patients under the age of 18 years, patients with chest depth of greater than 30 cm (to ensure

consistency in patient sizes), those patients weighing over 105 kg and patients who had 120kV CTPA protocol were separately evaluated. Patients who had CT angiogram initial or chest CT angiogram (other names of the same protocol) were not included in this study, as CT pulmonary angiogram had provided sufficient data for analysis. The data were presented in terms of statistical properties such as minimum, mean, and maximum radiation doses with confidence intervals. The study also presented the frequency distribution of the list of alternative findings on CTPA and the incidence of suboptimal examination. The details of this retrospective review are available in chapter 4, section one.

3.6.1.3: Justification of the Technique

Pulmonary embolism has varied clinical presentation symptoms such as dyspnoea and chest pain which are non-specific and may be seen with many acute respiratory diseases. Therefore when clinicians request CTPA, they aim not just to diagnose or exclude PE but to also identify or exclude alternative diagnoses. The optimal method to identify PE alternative diagnoses was to retrospectively review a large sample size of CTPA examinations; this was because of the ease of data collection, the accuracy of the results, and the difficulty of a prospective review with what was thought to yield similar results. Even though the retrospective review provided rich and detailed information, further confirmation of the findings was required. A questionnaire was presented to medical doctors to offer their opinion.

3.6.2: Stage Two: Questionnaires of Medical Doctors Regarding PE Differential or Alternative diagnosis

Senior clinicians were consulted in unstructured interviews to identify the opinions on PE differential diagnosis. Questionnaires were formulated bases on their opinions, and the senior medical doctors had further input into the question presented to medical doctors. Involvement was voluntary. A sizable number of medical doctors in the hospital were chosen, 40 doctors in total; however, 31 medical doctors returned the differential/alternative diagnosis questionnaire. Medical doctors were asked to rank the seven most common alternative diagnoses to PE that they thought caused pleuritic chest pain and dyspnea. The medical doctors were assured of anonymous survey responses to ensure honest and truthful answers with reduced bias. Only questions completed were utilized in the analysis. The sample size

was smaller than expected. The low questionnaire return rate is common in surveys as the bulk of medical doctors who receive questionnaires do not return them. This drawback was identified initially, and a preventive measure was taken to make sure most of the questionnaires were fully completed in subsequent research. Whilst this may bias the result, it was thought not to be significant as confirmation of findings with the retrospective review. The details of these questionnaires are available in chapter 4, section two.

3.6.3: Stage Three: Questionnaires of Medical Doctors Regarding CTPA Over-Ordering

The retrospective review identified a significant overuse in CTPA within this imaging department. 89% of CTPA patients were found to have had either no radiological abnormality or had an alternative diagnosis where chest radiographs are thought adequate for diagnosis. It was, therefore, essential to study and discover why these patients were having unnecessary CTPA. Hence an additional survey was given to medical doctors to identify the cause of over-ordering

This research project intended to determine the main contributors to CTPA over-ordering and overuse, and also the strategies to eventually device methods decrease unnecessary CTPA examinations.

Senior medical doctors were consulted in unstructured interviews to identify the issue with regards to over-ordering; after the initial interviews, questionnaires were prepared, the original senior medical doctors then had further input and the modified questions. The questionnaire was presented to medical doctors. Involvement was voluntary. A sample size comprised of 63 medical doctors were obtained, including intensive care doctors, general surgeons, radiologists, and emergency doctors. The surveys were given to doctors, and the survey was designed as a Likert scale, as shown in appendix II. The details of these questionnaires are available in chapter 4, section three.

3.7: Prospective Comparison Study of Standard CTPA Protocol vs Low Dose CTPA Protocol for Images Quality and Radiation Dose

This chapter contains two studies. Stage one study discusses prospective comparison study of standard CTPA protocol vs improved 80kV CTPA protocol for Images quality and radiation dose. Stage two study contains a qualitative testing survey of medical doctors on Image quality.

3.7.1: Stage One: Quantitative Testing: Prospective Comparative Study

3.7.1.1: Aim

In this study, a prospective comparative study was conducted comparing the two protocols: the standard CTPA protocol and the improved 80kV CTPA protocol before and after the introduction of the low dose CTPA protocol. The purpose of this was to test the effectiveness of radiation exposure with the intervention (low dose CTPA protocol). The research tested if the radiation exposure of improved 80kV is lower than the standard CTPA protocol.

3.7.1.2: Method

The study involved 100 patients with suspected PE who required CTPA. Patients underwent imaging on a Toshiba 320-row multi-detector in the absence of the software for radiation reduction, known as FIRST [abbreviation]. The study participants were categorised into control group A and low dose group B. Each of the control and test groups consisted of 25 women and 25 men patients. The two groups were chosen in a way that they have similar age and weight distribution. For example, the mean age of the participants in the control group A is 56.050±19.66 years, whereas this for the test group is 54.06 ±21.52. The mean weight of the participants in the control group A is 69.88±14.23 years, whereas this for the test group is 68.96 ±13.45

Group A included 50 patients who were allocated to the standard CTPA 100kV procedure with reconstruction algorithm-kernel FC 53 with tube current modulation, the image reconstruction process AID 3D standard, and an effective mAs of 215. This data was gathered prior to implementing a low dose CT pulmonary angiogram protocol. Group B was allocated to improved 80kV CTPA protocol with the image reconstruction process AID 3D strong, standard deviation setting of level 8 (Sure Exposure 3D), an effective mAs of 258,

and 80 kV, as well as the reconstruction algorithm-kernel FC 51 in the lung window incorporated with tube current modulation. To ensure the consistency of the two group, pair matching was conducted.

The number of patients in the studies has been driven by practical considerations and the availability of radiologists. The power of the sample size was calculated, and the sample size was found to be large enough for the findings to be generalised.

Besides, all the images were attained in a sole breath-hold and craniocaudally manner. The injection rate was similar between the patients; they will receive a 40-70mL iodinated contrast medium with a 50mL saline flush. Besides, an 18-G cannula with the cubital fossa will be utilised with a 4.5mL/sec flow rate through the dual-headed injector. An automated bolus tracking system will be formulated at 180HU and region of interest (RIO) positioned within the pulmonary trunk. Two experienced radiologists with over 8-year experience reported the studies. The acceptable standard to participate in this study was to be a medical graduate with qualifications accepted by the Royal Australian and New Zealand College of Radiologists with a minimum of 8 years of experience. The minimum requirements were based on previous studies' methodology, practical considerations and availability of the staff.

The image quality of both groups was evaluated using a 3-point scale. Images with no issue and/or minimal noise were rated with a score of 1(excellent image quality). Images with no issue but with slightly increased image noise were rated score 2(good image quality). Images with noticeable image quality issues and/or significant image noise are rated as score 3(Suboptimal image quality). In the case of disagreeing scores in the study group's subjective image analysis, where one radiologist said suboptimal, and the other disagreed, images were reanalysed, and consensus between the two radiologists was reached.

The study excluded patients under the age of 18 years, patients suffering from kidney failure with estimated Glomerular Filtration Rate (eGFR<30), and chest depth of greater than 30 cm or weigh over 105 kg. A region of interest was positioned at the pulmonary trunk to evaluate contrast enhancement, specifically to achieve the correct measurement in Hounsfield units (HU). Images that demonstrate a contrast enhancement with more than 210HU in the main pulmonary artery were accepted for having satisfactory contrast enhancement to detect PE[.173]. The images were then ranked as suboptimal or non-diagnostic in cases where the contrast enhancement was lower than 210 HU in the main

pulmonary artery or if the reporting radiologist graded the images as non-diagnostic or suboptimal. In the end, the radiologist provided an opinion on image quality.

The data were presented in terms of statistical properties, such as minimum, mean and maximum (with confidence interval) of radiation doses and contrast enhancement. The study presented the frequency distribution of the list of PE alternative/differential diagnoses.

The outcome variable, radiation dose and contrast enhancement are quantitative by nature. Hence, side by side box plot is presented to visualise the differences and to show the distribution of the radiation dose and contrast enhancement

A test of the hypothesis was conducted to test if significant differences exist between the mean of radiation dose 100kV protocol and improved 80kV CTPA protocol. For this purpose test, independent samples *t*-test with an unequal variance is utilised to compare the radiation doses of the improved 80kV CTPA protocol and standard protocol. Radiologist's findings on diagnostic confidence and image quality are presented to confirm or reject the hypothesis. The details of this prospective comparative study are available in chapter 5, section three.

3.7.2: Stage Two: Qualitative Testing: Survey of Medical Doctors

3.7.2.1: Aim and Method

Radiology consultants were interviewed with an unstructured interview format to identify key issues regarding image quality. Questionnaires were formulated on the basis of their opinions, and the interviewed radiologists had further input into the questions that were later presented to medical doctors. The final questionnaires (Appendix 1) were presented to 50 medical doctors. The purpose of the questionnaires was to assess the medical doctors' opinions on image quality, their impression and diagnostic confidence regarding 80kV CTPA with improved image noise reduction vs standard 100kV CTPA protocol.

Because of the small number of radiologists, this research decided to get a larger sample and also question the main imaging consumer, the emergency medicine doctors. This also helped determine whether the novel protocol is useful in examining PE in the emergency medicine context.

Medical doctors were called to witness contrast during CT examinations; they were then asked to evaluate images on the CT viewing screen. The doctors were then asked to fill out the questionnaires, as presented in Appendix 1.

To reduce bias, the medical doctors were not informed of the findings obtained from the case studies. Because of time constraints, some clinicians were approached to evaluate image quality and complete the questionnaires after the completion of the examination or when available.

The survey findings are presented in the context of the prospective comparison study, which was conducted in the first part of this study. The details of these questionnaires are available in chapter 5, section four.

3.8: Prospective Comparison Study of Standard CTPA Protocol vs Optimised Low Dose CTPA Protocol for Failure Rate with Open Mouth Breath-hold and Higher Injection Rate

3.8.1: Quantitative Testing: Prospective Comparative Study

3.8.1.1: Aim

This study intends to decrease radiation dose, suboptimal image quality and improve contrast enhancement among patients undergoing CT Pulmonary Angiography (CTPA) with a suspected Pulmonary Embolus (PE) by utilising improved 80kV CTPA protocol, an increased injection rate and gentle breath-hold with an open mouth acquisition method.
The study aims to determine whether the improved 80kV CTPA protocol with gentle breath-hold with open mouth technique effectively decreases suboptimal CTPA examination in patients weighing below 105kg.

3.8.1.2: Method

This study received approval from the Australian National University and the Australian Capital Territory Public Hospital Ethics Committee Review Committee. One hundred forty patients were enrolled before undergoing CTPA and split into two separate groups of 70 (Group A and Group B). Peer matching was utilised to select patients to form a cohort of comparable patients.

Group A was allocated to a routine standard of 100kV CT pulmonary angiogram protocol; they were required to take a deep breath and hold it instantaneously before undergoing the CT scanning as per standard practice. A reconstruction algorithm-kernel FC53 with tube current modulation was used in combination with an image reconstruction protocol AID 3D standard and an effective mAs of 215 also as per standard practice. The scanner automatically instructed them to perform the breathing instruction. The data was recorded prior to the implementation of the low dose CTPA protocol for group B.

Group B was allocated to the low-dose CTPA protocol with the image reconstruction process AID 3D Strong and a standard deviation of the tube current level 8 (Tradename: ‘Sure Exposure 3D’). An effective mAs of 258, and tube voltage of 80kV with tube current modulation. The reconstruction algorithm utilised a kernel FC51 was utilised to provide reduced noise. A larger cannula with a higher minimum injection rate of 4.5ml/s was utilised to increase the CT contrast enhancement. Patient education on breathing was implemented

with active coaching and relaxation techniques to achieve a gentle breath-hold with an open mouth to decrease Valsalva and motion artefact.

Peer matching was utilised; both control and test groups consisted of 35 female and 35 male patients. The two groups were to have comparable age and weight distributions. The mean age of the participants in control group A was 60.0±19.98 years versus 57.5 ±20.67 for Group B. The mean weight of the participants in group A was 68.94±12.55 years versus 68.54 ±13.22 for Group B.

All the patients were scanned on a 320-row multi-detector Toshiba Aquilion One Genesis Edition, without 'FIRST', a propriety software used for radiation reduction. They were also given 40-70mL iodinated contrast medium iopromide 370 mg/mL (Bayer, tradename Ultravist) with 50mL saline flush as per standard protocol with contrast medium dosing based on weight. The study used an 18-G cannula inserted in the cubital fossa. A minimum flow rate of 4.5 mL/sec flow rate was used with an unmodified dual-head injector. An automatic bolus tracking structure was utilised with a scanning trigger with 180 HU in the pulmonary trunk, as is common practice.

For this study, exclusion criteria were: patients under the age of 18 years, patients with renal impairment defined as estimated glomerular filtration rate (eGFR) <30 ml/min/1.73m^2, chest depth of greater than 30 cm, or weigh over 105 kg. The last two exclusion criteria were set as they are parameters for using higher tube voltage.

A region of interest was positioned at the pulmonary trunk to evaluate contrast enhancement, specifically to achieve the correct measurement in Hounsfield units (HU). The minimum ROI size was 5 mm^2. Images that demonstrated a contrast enhancement with more than 210 HU in the main pulmonary artery were accepted for having satisfactory contrast enhancement to detect PE. The images were considered suboptimal or non-diagnostic when contrast enhancement was less than 210 HU in the main pulmonary artery or when the two reporting radiologists graded the images as non-diagnostic or suboptimal. In the case of disagreeing scores in the study group's subjective image analysis, where one radiologist said suboptimal, and the other disagreed, images were reanalysed, and consensus between the two radiologists was reached.

The data were presented in terms of statistical properties such as minimum, mean and maximum (with confidence interval) of radiation doses and contrast enhancement. The study also presented the frequency distribution of the list of PE differential diagnoses. A side by

side box plot is presented to visualise the differences and distribution of the radiation dose and contrast enhancement.

A hypothesis test was conducted to test if significant differences exist between the mean of radiation dose 100kV protocol and improved 80kV CTPA protocol. For this purpose, a test independent sample t-test with unequal variance was utilised to compare contrast enhancement and the improved 80kV CTPA protocol's radiation doses versus the 100kV standard protocol. The alternative hypothesis is tested using a test for equality of proportions with continuity correction validated that the rate of suboptimal examinations from the low dose CT pulmonary angiogram is significantly lower than that from the 100kV protocol. The details of this prospective comparative study are available in chapter 6, section one.

3.9: Validity and Reliability of the Methods

The validity measures the extent to which the tool we used measures what is intended to measure, whereas reliability is consistency with which a measuring instrument produces a specific result when the entity measured has not changed [126]. In this study, it was acknowledged that when comparing two groups, both validity and reliability were essential, and without them, results obtained are uninterpretable, and it would be challenging to draw a conclusion.

In the quantitative studies where a prospective comparison design was utilised to minimise the impact of bias, it also utilised equivalent sample sizes and used pair matching by selecting patients with similar weights, ages, and gender. In the imaging interpretative phase, standardised image sets were utilised, adequate viewing conditions and equal durations for interpretations were provided to ensure unbiased and comparable results.

In the image reporting, this study used consensus among reporting radiologists. Having consensus among reporting radiologists was aimed to provide internal validity and reliability. It was also in place in order to have consistency. Hence, when one radiologist said suboptimal, and the other disagreed, images were re-analysed, and the two radiologists reached a consensus. This approach was driven by practical considerations. A better way of reaching a recognised consensus was having a third radiologist break a deadlock and help lessen preference bias. A third radiologist was not available during the time of the study.

The power calculation is essential for sample size. The four ingredients required for a sample size calculation are significance level (0.05), power (0.80), minimum clinically important difference in the outcome, and measures of variability in outcome by treatment group in both treatment and control. In the prospective comparison studies, the required sample size was power calculated and presented the respective part of the thesis. In most cases, the sample size was large enough for the findings to be generalised.

In the qualitative studies, surveys questions were designed with consideration of wording and order of the questions after clinician input; this was done to ensure both validities of the question and reliability of the results and applicability of the question for clinician and study aim. The survey's visual layout used the same format and a Likert rating scale for respondents that have been extensively utilised in opinion surveys and academia[126].

The questionnaire validity and reliability was established by having two experts who understood the topic read through the questionnaire. The experts assessed whether the questions were effective in assessing the topic under examination. The experts also checked common errors that could lead to confusion. They also assessed the correlation between questions and answers. A pilot test was conducted with 10 participants. Responses were assessed for consistency between the participants and to check whether the medical doctors filled the survey appropriately to the questions. The standard test included checking the reliability of the answers and whether responses were consistent from one to the other. After reviewing the reliability of the survey, some questions found not to be reliable were removed.

Additional strategies utilised to ensure the validity of the questionnaires included: Asking respondents to provide sufficient details on the answers and seeking feedback from the respondent medical doctors to ascertain whether they appropriately interpreted the question. The results were also checked with senior medical doctors to see if they agreed with the conclusion based on their experience.

The aim of his research was to discover the current opinion of medical doctors in differential diagnosis, image quality, and CT overuse. A simple above validity and reliability test was established. According to the Australian National University statistical consulting unit, questionnaires do not require highly developed reliability and validity for insurance. They are newly designed, highly targeted questions intended to picture the medical doctors' current views.

This study acknowledges that this design does not entirely eliminate bias; however, when this is thought to affect the research, it is taken into account in the discussion and conclusion.

3.10: Consent

The participants were asked to voluntarily offer consent if willing to participate in this research project, see Appendix 1V. Adequate information concerning the research aim and risks and the importance of the study were offered. The research objectives were explained, and patients were provided room to ask for any questions and deliberate concerns or issues they had before they provided their responses. The aim was to establish a mutual understanding between the patients and the researcher. Thus, all participants were assured that this study did not result in any legal, social, economic, psychological, or physical harm.

Chapter 4: Retrospective Review of CT Pulmonary Angiogram Examinations and Questionnaire of Medical Doctors

Chapter four contains three sections. Section one discusses a retrospective review, which aimed to understand better PE differential diagnosis and the problem of over-utilisation of CTPA. Section two discusses questionnaires to senior emergency medical doctors (registrars and consultants) to provide their opinions regarding the differential diagnosis or alternative diagnoses they considered when assessing for pulmonary embolus, chest pain and dyspnoea. Section three discusses questionnaires to senior clinicians to identify the factors contributing to CTPA over-ordering.

4.1: Section One: Retrospective Review of CT Pulmonary Angiogram Examinations

4.1.1: Aim

The retrospective review aims to understand better the problem of CTPA over-utilisation and reasons for over-ordering, including the differential diagnosis of chest pain. The retrospective review would allow us to assess the baseline of CTPA examinations at this facility, incidental findings, and suboptimal studies.

The retrospective review involved identifying and collating patient records to ascertain the percentage of positive pulmonary embolism, the number of suboptimal studies, alternative or differential diagnosis for chest pain or dyspnoea on CTPA and evaluated the mean effective dose (mSv) when the standard 100kV was utilised. One of the reasons this study aims to understand the differential diagnosis of chest or dyspnoea on CTPA was to ensure that when a low dose CTPA protocol is designed and introduced, it will be able to identify the differential diagnoses. This is important because doctors are looking for the cause of the symptoms; they want to exclude pulmonary embolism, but crucially they also want to identify an alternative diagnosis.

4.1.2: Method

A retrospective review was undertaken. CTPA reports from the centralised Picture Archiving Communication System (PACS) system from examinations conducted between 1st of April 2018 to 31st of March 2019 (1 year period) were extracted and analysed. 748 CTPA

scans among patients with suspected PE were retrospectively examined to identify the incidence of pulmonary embolism diagnosis and the most frequent incidental diagnoses. The data were presented in terms of statistical properties, such as minimum, mean, and maximum radiation doses with a confidence interval. The study presented the frequency distribution of the list of PE differential diagnoses and incidental findings.

4.1.3: Overall Finding

Seven hundred forty-eight exams were reviewed (448 F: 300 M). It was found that only 82 cases of PE were identified out of the 748 CTPA scans (11%). 251 patients had differential diagnoses or incidental finding, the most frequent were: pneumonia/infection 8.5% (64/7848), emphysema 6% (46/748), atelectasis/collapse 4.5% (33/748) pulmonary nodules 4% (31/748). Many less common entities, less than 2% incidence each, were also detected; these included: asbestosis/pleural plaques, lymphadenopathy, rib fractures, lung mass, coronary calcification, bronchiectasis, pleural effusion, pulmonary oedema, pulmonary hypertension, pneumoperitoneum and pericardial effusion. These differential diagnoses or incidental findings are presented in table 4.1.

Moreover, the findings obtained show that 415 out of 748 patients (55%) had neither pulmonary embolism nor an alternative diagnosis/incidental finding identified in the report. Furthermore, seven patients were noted to be pregnant in the clinical history at the time of the scan, out of 748, which equates to < 1% incidence. Higher positive PE cases were also identified in the winter months cases were (May=13, June =8, July =13; August =16); conversely, less positive PE cases were detected in summer months compared to the winter period (December = 3, January =4, February= 3, March 2 cases only).

4.1.3.1: Effective Radiation Dose

The 100kV pulmonary angiogram in the imaging department had a minimum effective radiation dose of 1.3mSv, a maximum of 7.12 mSv and the mean was 3.06mSv. The standard deviation was 0.54.

4.1.3.2: Suboptimal Images

The retrospective review of radiologist's reports and image quality discovered 38 out of the 748 examinations were suboptimal studies (5% incidence). It was impossible to recall and ask the cause of suboptimal to the initial reporting radiologists; some are not working for the reporting company anymore.

The most frequent contributors to suboptimal studies that were noted were low contrast enhancement, motion artefact and multifactorial technique failure (which assumed to include cannula failure, limited venous access, and inadequate flow rate). The images were considered suboptimal or non-diagnostic when contrast enhancement was less than 210 HU in the main pulmonary artery[173]or when the reporting radiologist graded the images suboptimal.

The study retrospectively reviewed 59 patients who were excluded from the standard CTPA analysis because they had 120kV. In the 120kV protocol, 14 out of 59 had suboptimal examinations, primarily as a result of low contrast enhancement and motion artefacts. A notable percentage (24%) of suboptimal scans were presented within this protocol despite the small number of large patients who went through a 120kV process within the department of imaging. Iodinated contrast enhancement decreased when a high tube voltage of 120kV was used because high tube settings take attenuation farther away of iodine K-edge at 33keV.

Table 4. 1: Alternative and incidental findings on CTPA.

Alternative diagnosis and incidental findings	Number
Normal exams – no alternative listed	415
Pulmonary Embolism	82
Pneumonia/infection	64
Exacerbation of emphysema	46
Atelectasis/collapse	33
Pulmonary nodules	31
Lymphadenopathy	10
Pleural effusion	9
Mass	9
Pulmonary oedema	7
Coronary calcification	7
Bronchiectasis	5
Rib fracture/s	3
Asbestosis	3
Pulmonary hypertension	3
Inflammatory changes	3
Lymphangitic carcinomatosis	3
Pulmonary fibrosis	3
Pericardial effusion	2
Aortic Dissection	2
Mesothelioma	2
Myeloma	1
Mosaic attenuation	1
Ground-glass opacity	1
Airway disease	1
Pneumothorax	1
Pneumoperitoneum	1

The most common incidental findings were pneumonia, emphysema and atelectasis. They all cause chest pain and dyspnoea, which can appear as PE.

4.1.3.3: Discussion on approaches to distinguish from PE from the three most Common Alternative or Differential Diagnoses on CTPA

The following discussion highlights the major clinical differences between the PE and pneumonia, emphysema and atelectasis. In the retrospective review pneumonia, emphysema and atelectasis were the most common alternative diagnoses on CTPA when looking for PE. This section will review these differential diagnoses based on clinical presentations, signs and symptoms, and radiographic features. The following sections describes clinical approaches to distinguish pneumonia, emphysema, and atelectasis from a PE.

4.1.3.4: *i).* Pneumonia

Pneumonia was the most common alternative diagnosis that contributed to dyspnoea and pleuritic chest pain. The retrospective review found that 64 out of 748 (8.5%) of the cases had pneumonia findings on CTPA. What is the key difference in clinical presentation between pneumonia and PE?

In pneumonia, often patients experience an insidious onset of worsening shortness of breath, cough (often productive of purulent sputum but can be non-productive), fevers, chills with rigours or night sweats, pleuritic chest pain (sharp, stabbing pain that is worse on inspiration), lethargy, malaise, nausea and fatigue. They may have been in contact with someone who was also unwell (and hence transmitted the infection such as influenza or there may be specific occupational exposures, such as exposure to air-conditioning or contaminated boiler systems/showerheads in the case of Legionella pneumonia, or exposure to birds droppings in the cases of Chlamydia psittaci pneumonia for example.

On clinical examination, there is often fever, desaturation and need for supplemental oxygen, tachypnoea with increased work of breathing, sometimes respiratory distress, tachycardia and hypotension if the patient is septic. If the patient is septic, they may have poor peripheral perfusion with reduced capillary refill time, confusion, or altered consciousness level (if severely septic or hypoxic). Auscultation examination finds harsh bronchial breath sounds in areas of the consolidated lung or often just crackles. There may be dullness to the percussion of the chest wall.

Laboratory findings may show respiratory failure on arterial blood gas with a low partial pressure of oxygen (paO2) and often low paCO2 if the patient is tachypneic (sometimes they may have hypercapnia with high paCO2 in the case of Type 2 respiratory failure when the patient is drowsy and not ventilating well or if they have underlying chronic airways disease such as COPD or sleep apnea). The lactate level is also elevated in patients with infection

and pneumonia (often >2mmol/L). Often the patient has an elevated white blood cell count (usually elevated neutrophil count if bacterial pneumonia) or can have elevated monocyte or lymphocyte count in the case of viral pneumonia, conversely elevated eosinophil count occur in asthma or parasitic infections. Elevated C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR) is common. In the case of severe infection and sepsis from pneumonia, they may develop multi-organ failure with deranged liver function tests or acute kidney injury (with a rise in the serum creatinine level). Blood culture and sputum culture tests are important for microbiological diagnosis, along with nasopharyngeal swabs for viral PCR to assess for influenza, respiratory syncytial virus, etc. Urinary antigen tests may be used for atypical organisms such as Legionella, Chlamydia or Mycoplasma. Serology tests can be used for atypical organisms. Sputum cultures are crucial for the detection of Mycobacterium tuberculosis (identification of acid-fast bacilli, but PCR can also be used).

A blood test may demonstrate an elevated white blood cell count, elevated neutrophil count if bacterial pneumonia, elevated monocyte or lymphocyte count in the case of viral pneumonia, or elevated eosinophil count in asthma. CRP is also raised, as discussed earlier. Blood culture and sputum culture tests are important for microbiological diagnosis, along with nasopharyngeal swabs for viral PCR to assess for influenza, coronavirus, RSV, etc.

Electrolytes, D-dimer, biochemistry, C-reactive protein (CRP), urea, and full blood count are vital to distinguish between pneumonia and other acute respiratory ailments. In streptococcus pneumonia, the markers of inflammatory are considerably increased while the erythrocytes sedimentation rate, abbreviated as ESR is anticipated to be higher than 100mm/hr. The CRP can be significantly increased, sometimes to greater than 100mg/L. CRP is a valuable blood test that attempts to measure inflammation and infection but can lag behind clinical findings. Depending on the history, if CRP is not considerably increased, it may be a cause other than pneumonia, and thus the treating clinician should consider a differential diagnosis[75].

A chest x-ray is often normal in pulmonary embolism, whereas you can often see consolidation (confluent, lobar or bronchopneumonia pattern) or an associated parapneumonic effusion or empyema in cases of severe pneumonia. The exception to this is that in atypical or viral pneumonia, where sometimes the chest x-ray may initially be normal but often progresses over days to become abnormal with consolidative changes[174-179].

If the chest is normal on the first presentation, it is recommended to be retaken after 2 to 3 days as pneumonia can develop later. When changes are seen on a chest x-ray, it is recommendable to repeat the chest x-ray after five weeks to identify longstanding changes

or exclude malignancy. A chest x-ray has moderate sensitivity but poor specificity; hence chest x-ray findings can lag behind clinical presentation[180].

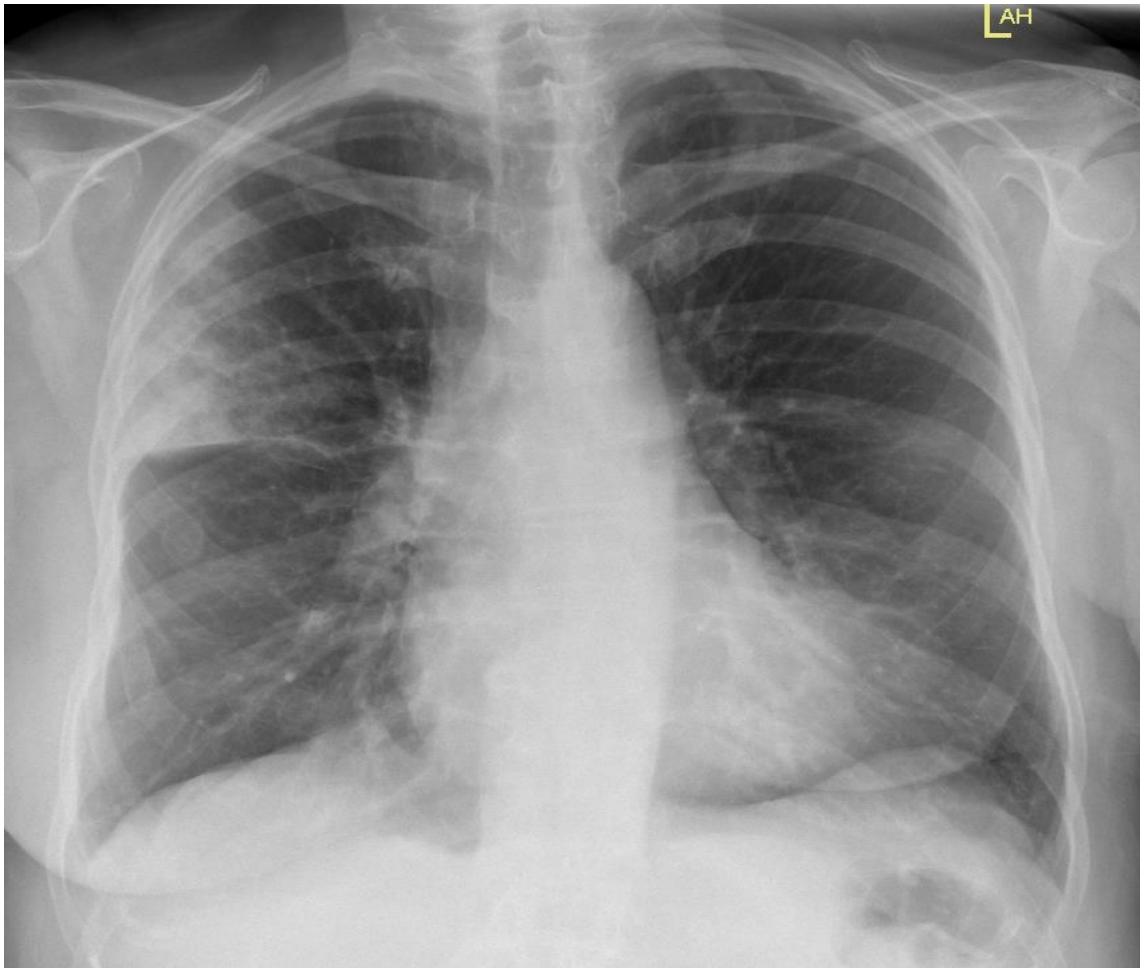


Figure 4. 1: Lobar pneumonia is in the right upper lobe, the most common type of pneumonia.

The above patient had a low dose CT pulmonary angiogram after the chest radiograph, which demonstrated atypical pneumonia-related consolidation in the right upper lobe.

In some cases, it is difficult to distinguish between mild pneumonia and PE. Patients with mild pneumonia often only have very mild symptoms at the presentation, which can mimic PE, one such case demonstrated in the figures below; this is the same patient with chest x-ray in figure 4.1. Hence, it should be aware of this mild pneumonia

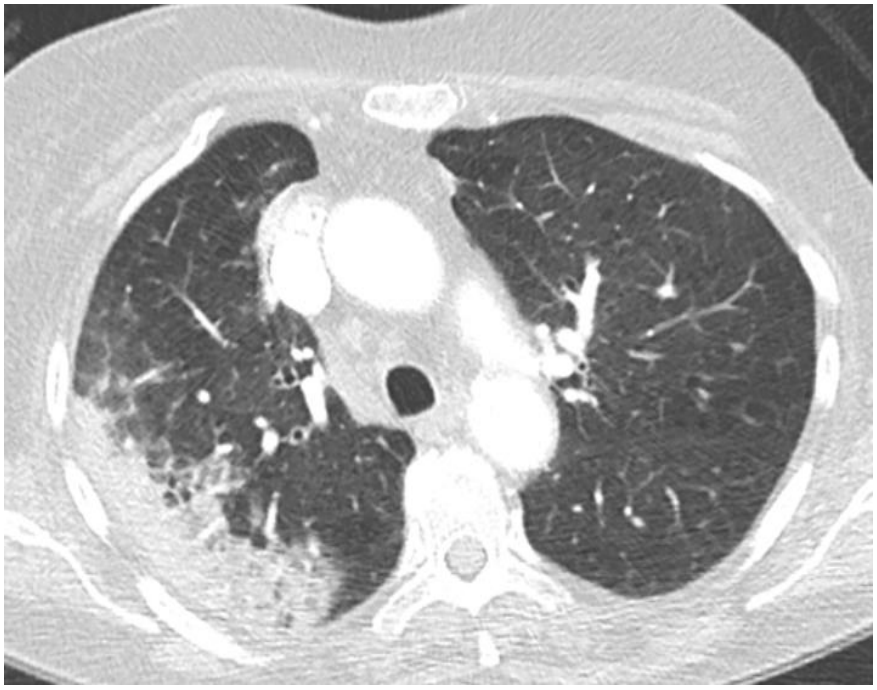


Figure 4. 2: Pneumonic consolidation in the right upper lobe in a patient presented with mild chest pain.

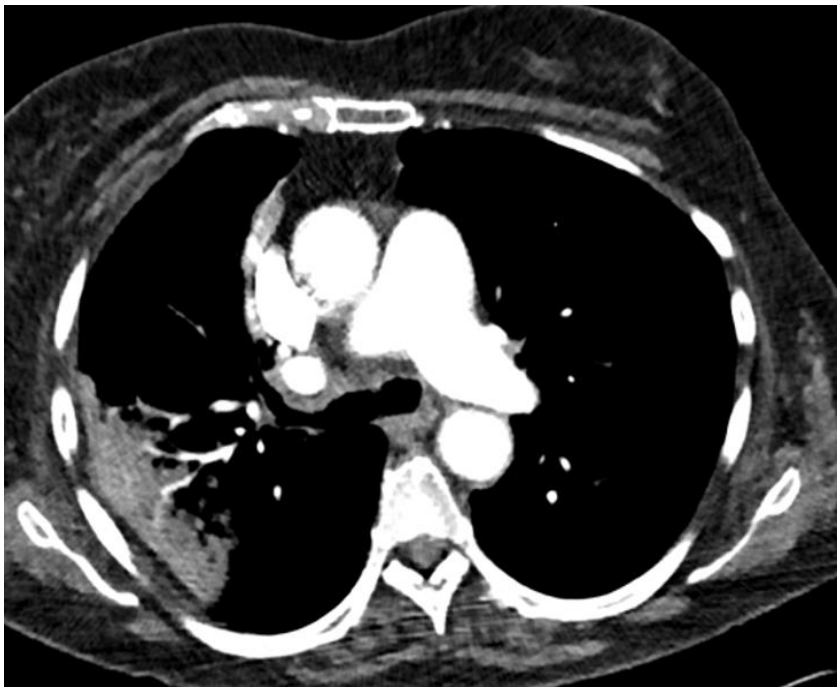


Figure 4. 3: Excellent contrast enhancement of lower tube voltage of a patient presented with mild chest pain.

4.1.3.4.1: Other Tests

Blood culture examination should be conducted on all septic patients, most often those with moderate to severe pneumonia. To treat the pathogen, clinicians initially utilise broad-

spectrum antibiotics and narrow down treatment once a pathogen is identified. The most frequent pathogen forms are outlined in the table below.

Table 4. 2: The most common pathogen types that cause pneumonia[181].

Pathogen type	common microbial of pneumonia
Virus 20%	Common is influenza. Uncommon: parainfluenza, adenovirus, rhinovirus, metapneumovirus.
Bacteria 75%	Typical: streptococcus pneumonia 50%, haemophilus influenza 5%, staphylococcus aureus 5%, gram negative rods <5%, Atypical: mycoplasma 10%, chlamydophila pneumonia 10%, legionella pneumonia <5%.

4.1.3.4.2: Management

For low-risk patients and those with low CURB-65 scores, home care is suitable. These patients are treated with oral antibiotics and followed up by their GPs; imaging is also seldom conducted beyond the chest radiograph.

For moderate pneumonia or those patients with elevated risk on CURB-65 1-2, the simplest initial treatment is supplemental oxygen either via nasal prongs or facemask. The treatment aim is to maintain saturation at approximately 95%. Intravenous fluids are also administered to hypotensive or dehydrated patients. Antibiotic treatment depends on the seriousness of pneumonia and is most often given orally. In moderate severity pneumonia, CRB-65 of 1-2, it is worth noting that there is a 9% mortality. Sputum tests and blood culture are also usually taken.

In severe pneumonia, where the CURB-65 is between 3-4 and has a high mortality rate, hospital admission is often required to a high dependency unit or intensive care unit. Patients undergo sputum and blood culture tests. Some patients undergo bronchoscopy for sputum sampling. IV antibiotics with broad-spectrum are given. Cross-sectional imaging is also often conducted to exclude non-infective pathologies such as cryptogenic organising pneumonia[181, 182].

4.1.3.5: Coronavirus Pneumonia

COVID-19 commonly presents as dyspnoea leading to increased utilisation of CTPA recently; it has a characteristic chest x-ray appearance. It often causes an interstitial pneumonitis pattern that appears similar to an interstitial lung disease that is usually most

severe at days 7-10 of the disease. In COVID-19 cases, CTPA clearly demonstrates consolidation or ground-glass pattern of changes that are usually multifocal and bilateral lesions. Several current studies reported overlap between acute respiratory syndrome coronavirus and PE[183-192]. Dyspnoea is very common with coronavirus. Furthermore, elevated D-dimer values were reported in up to 43% of patients with acute respiratory syndrome coronavirus, with higher D-dimer values seen in patients with more severe COVID 19 disease[193]. Hence, in the context of coronavirus, PE diagnosis is highly challenging. Whyte et al. (2020) from King's College London found that in patients with confirmed acute respiratory syndrome coronavirus, amongst those who had a clinical suspicion for pulmonary embolism, more than one-third of CTPA examinations were positive for PE[194].

A recent study from the New England Journal of Medicine established that 86% of chest CT examinations were abnormal among COVID 19 patients at the time of admission[195]; Medical doctors are aiming to diagnose PE or see a ground-glass pattern of changes of coronavirus; this is thought to be the main reason for the increasing CTPA request. The overlap between PE and COVID 19 has been extensively discussed by current studies[177, 196-201].

4.1.3.6: *ii*). Emphysema

Emphysema exacerbation was the second most common alternative diagnosis that contributed to dyspnoea and pleuritic chest pain. In the retrospective review, 46 out of the 748 cases, which represented 6%, had the alternative diagnosis of emphysema. What is the key difference in clinical presentation between acute exacerbation of emphysema and PE?

Acute exacerbation of emphysema can sometimes be complicated by pneumonia or PE as well. However, patients often have a long-standing history of COPD, smoking and frequent hospital presentations with exacerbations. The condition is often worse with a longer smoking history. In rare cases, there may be a history of alpha-1 antitrypsin deficiency. Often these patients have a long-standing history of emphysema or bronchitis from smoking and present with worsening shortness of breath, reduced exercise tolerance and cough. There is a significant overlap between COPD and pneumonia, with infective exacerbations (caused by viruses or bacterial infection) being a common cause for presentations; non-infective exacerbations due to the disease process itself also occur. Infective exacerbations often have productive purulent sputum, fever/chills, myalgias/arthralgias or preceding viral URTI symptoms. Before any CT examination, important tests include blood and sputum cultures, nasopharyngeal swabs for viral PCR tests, chest x-ray and blood tests (CRP is often elevated in infective exacerbations and normal or low in non-infective exacerbations).

Chest x-ray radiographic findings of emphysema are flattened hemidiaphragm, hyper lucent lung, increased lung volumes, increased lung markings with decreased vascularity (figure 4.4).

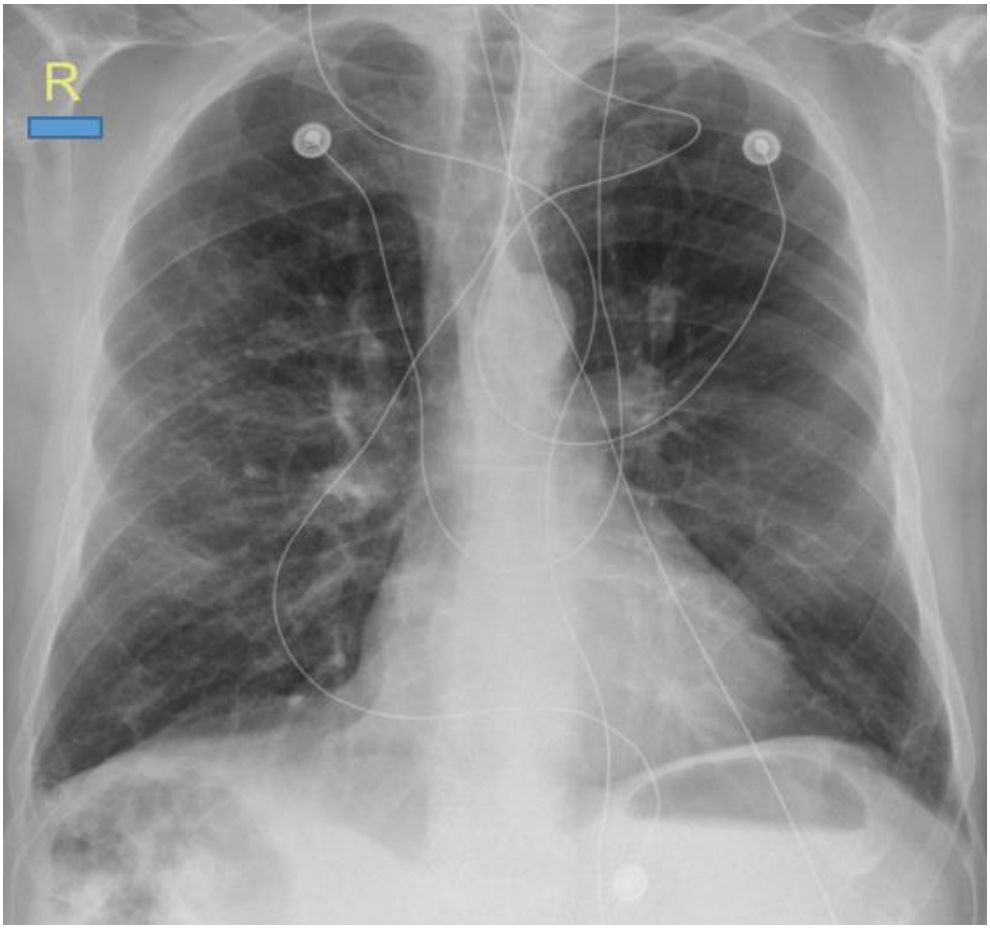


Figure 4. 4: Emphysema in the lungs with reduced vascularity and flattening of the Hemi diaphragms.

A high-resolution chest CT scan is the most accurate and sensitive imaging modality for diagnosing emphysema. It can identify the degree, pattern, and presence of the disease. Some of the CT findings are the presence of areas of low attenuation or lucencies distributed without defined margins, as illustrated in the figure below.

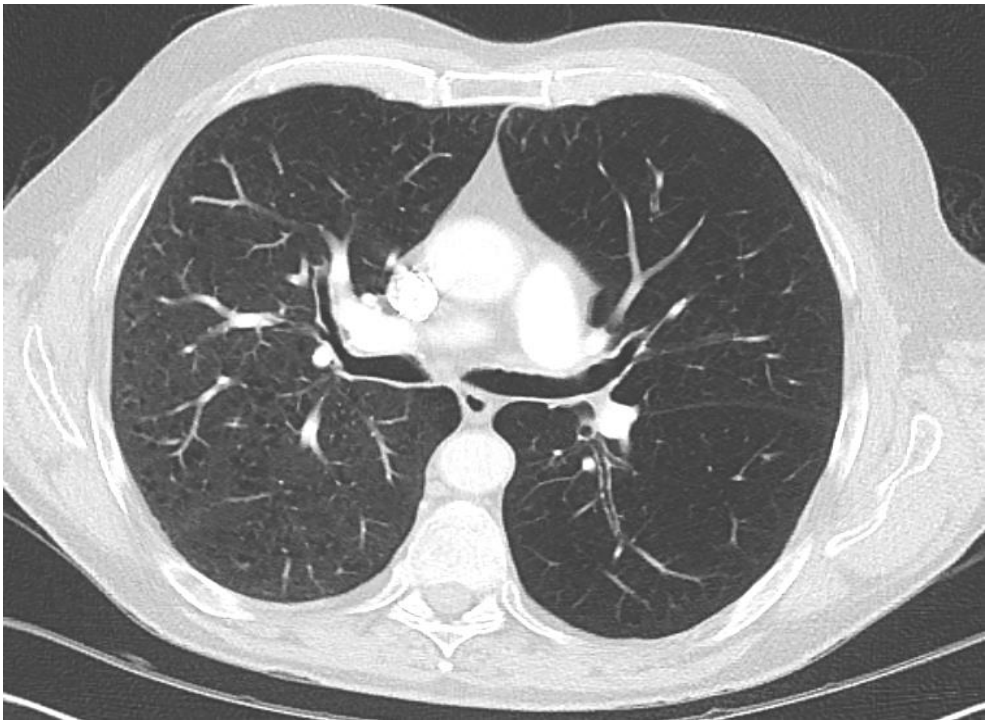


Figure 4. 5: Excessive low attenuating emphysema in the lung in a low dose CT scan.

It is important to know that PE may contribute to emphysema exacerbation. Hence, with the absence of infection, symptoms such as cough and fever, pleuritic chest pain, and sudden breathlessness may be related to acute PE exacerbation. This has been confirmed by the result obtained from a meta-analysis of approximately 880 patients with undefined COPD acute exacerbation; in this study, 16% of patients had a diagnosis of pulmonary embolism. Among them, 68% of the PE was discovered with the main pulmonary, interlobar, and lobar arteries [202],[174].

The prevalence of PE among patients suffering from acute exacerbation of COPD has been reported by serval studies[203-214].

Management may include ceasing smoking and taking bronchodilators, for instance, Salbutamol, regularly to treat symptoms. Other drugs include long-acting B2, for example, tiotropium. Notably, tiotropium is also used to enhance the quality of life and decrease the occurrence of exacerbations. Because the infection is the most common exacerbating factor, patients are often given short term antibiotic therapy[75, 182].

4.1.3.7: *iii).* Atelectasis

Atelectasis was the third most common alternative diagnosis that contributed to dyspnoea and pleuritic chest pain. In the retrospective review, 33 out of the 748 cases, representing 4.5%, had incidental atelectasis findings. What is the key difference in clinical presentation between atelectasis and PE?

Atelectasis is not life-threatening. This condition is prevalent in hospital patients post-operatively or patients who are not very mobile and do not do much deep breathing (common with associated rib fractures). Other causes are endotracheal tube malposition, bronchogenic carcinoma, aspiration and foreign bodies, immobility, and mucus plugs are believed to be the most causes of atelectasis [215-217]. Often there may be no clinical findings, but patients may desaturase on room air (which improves with deep breathing or supplemental oxygen). On examination, there may be basal crackles.

Risk factors include lung diseases such as chronic obstructive pulmonary diseases, general anaesthesia, recent surgery, older age, stroke or general bad medical condition.

4.1.3.7.1: Chest X-Ray

The best is to perform a chest x-ray which often shows linear bands of atelectasis or major collapse. Chest x-ray shows important features such as volume loss, displacement of hila, diaphragm, fissures, and sharp patchy opacity obscuring the lung vessels. In some instances, atelectasis may present with the same appearances as pneumonia, particularly when severe it may appear as lobar consolidation. Lateral chest films are used to assess the degree of volume loss within the collapsed lung. Hiatus hernias may also resemble lower lobe atelectasis[218,219]. Atelectasis showing collapsed lung to linear bands of atelectasis are demonstrated below in Figures 4.6 to 4.11.

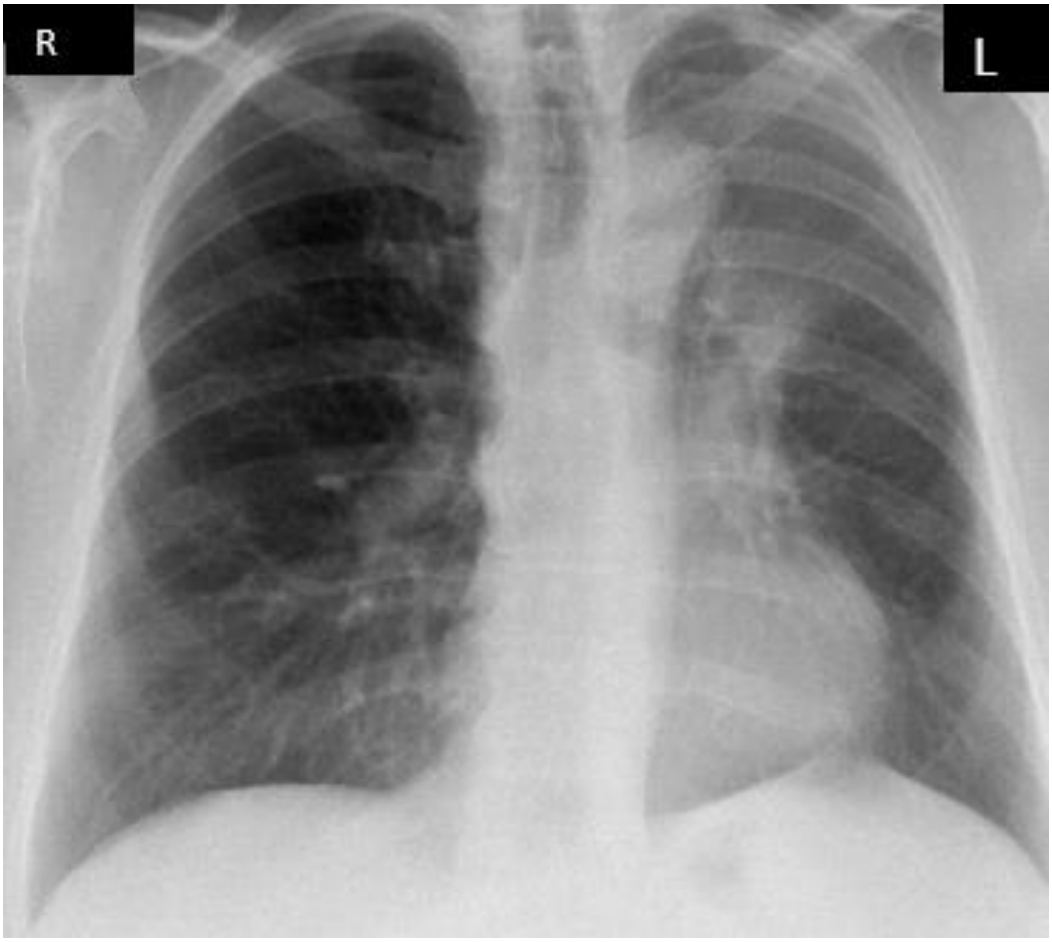


Figure 4. 6: Sharp patchy opacity on the left upper zone indicate a collapse of the left upper lobe.

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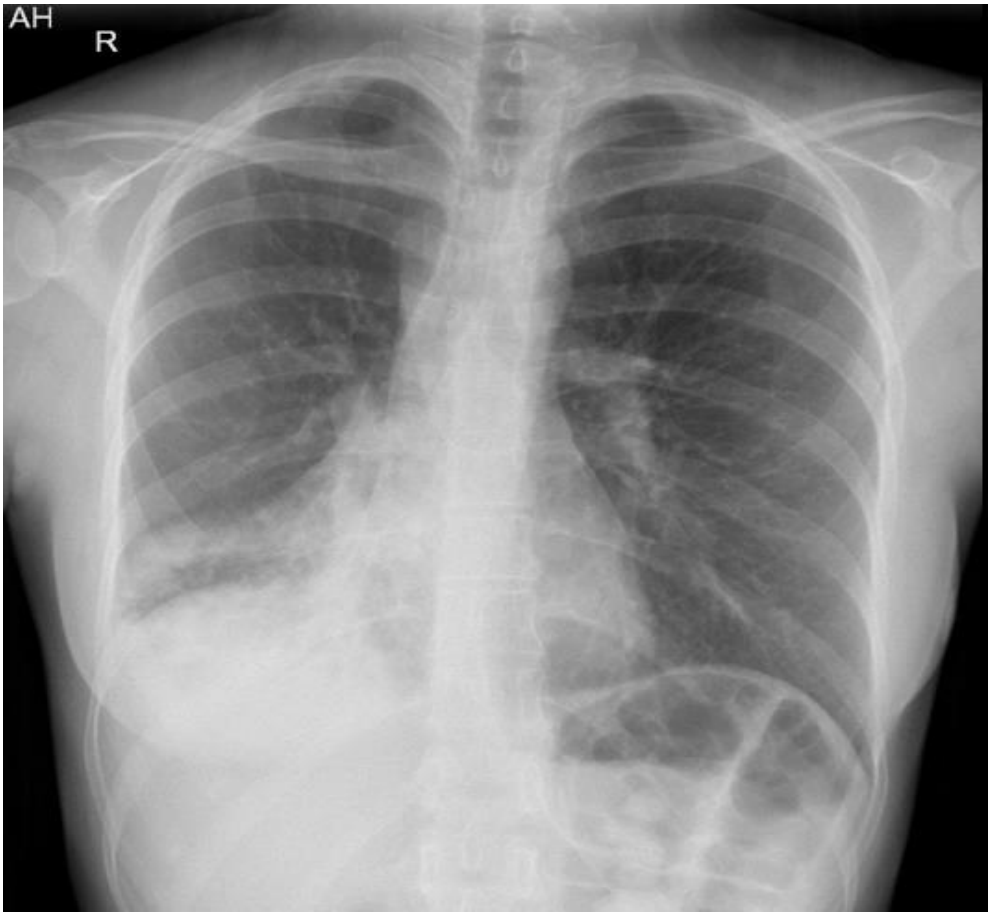
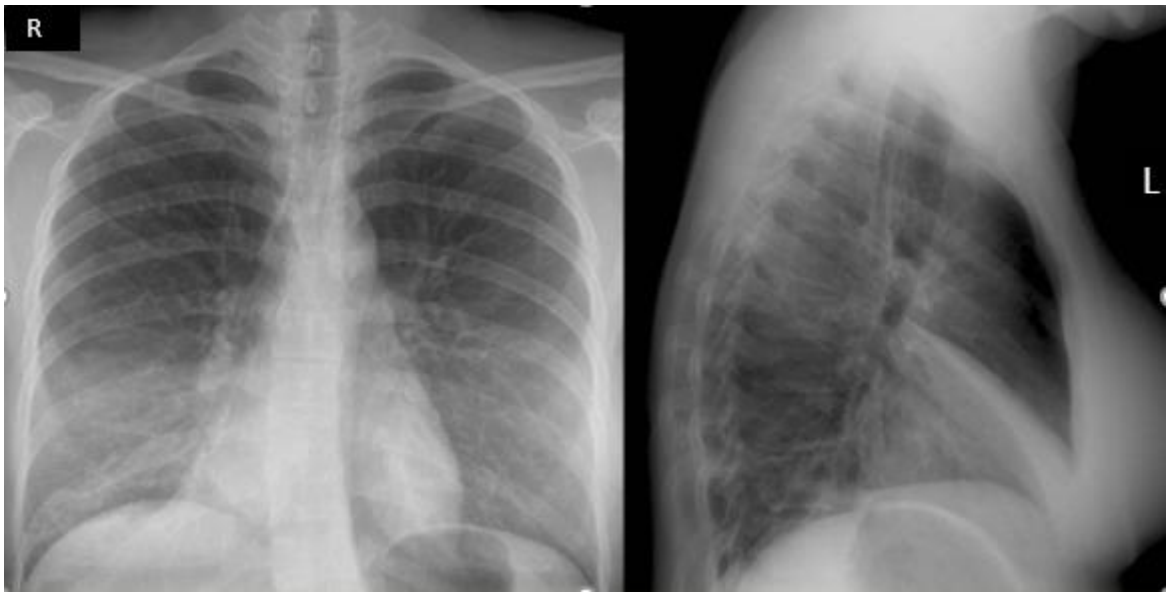


Figure 4. 7: Righ lower lobe atelectasis with increased retrocardiac opacity silhouetting left hemidiaphragm, hilum shifts downward.

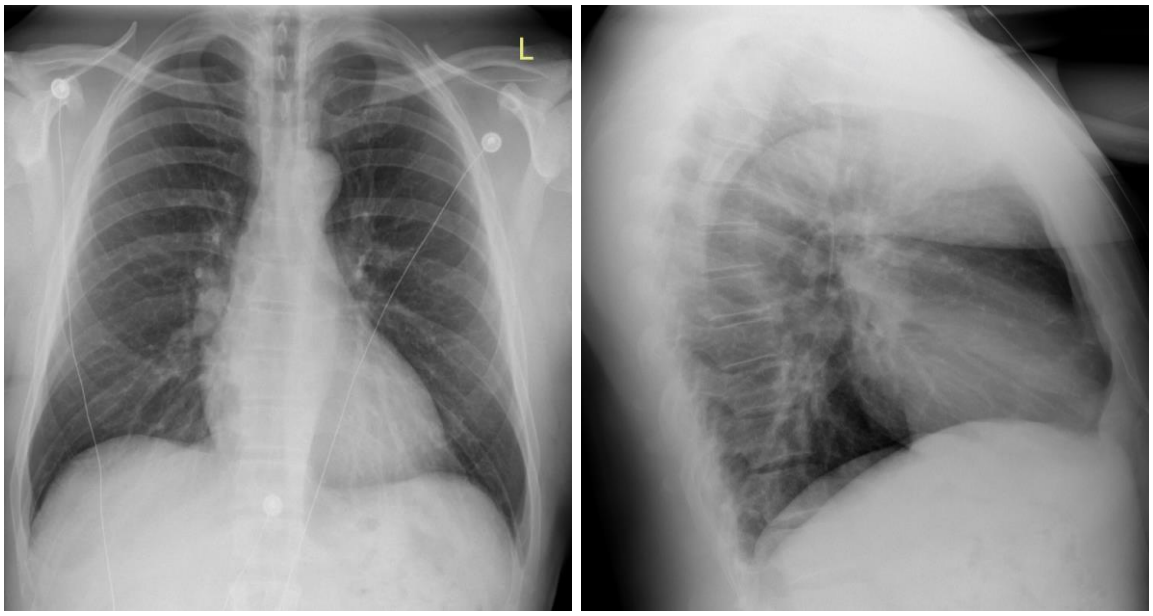


a b

Figure 4. 8: Chest x-ray with right middle lobe atelectasis, there is sharp patchy opacity in the image (a), and opacity with volume loss in (b).

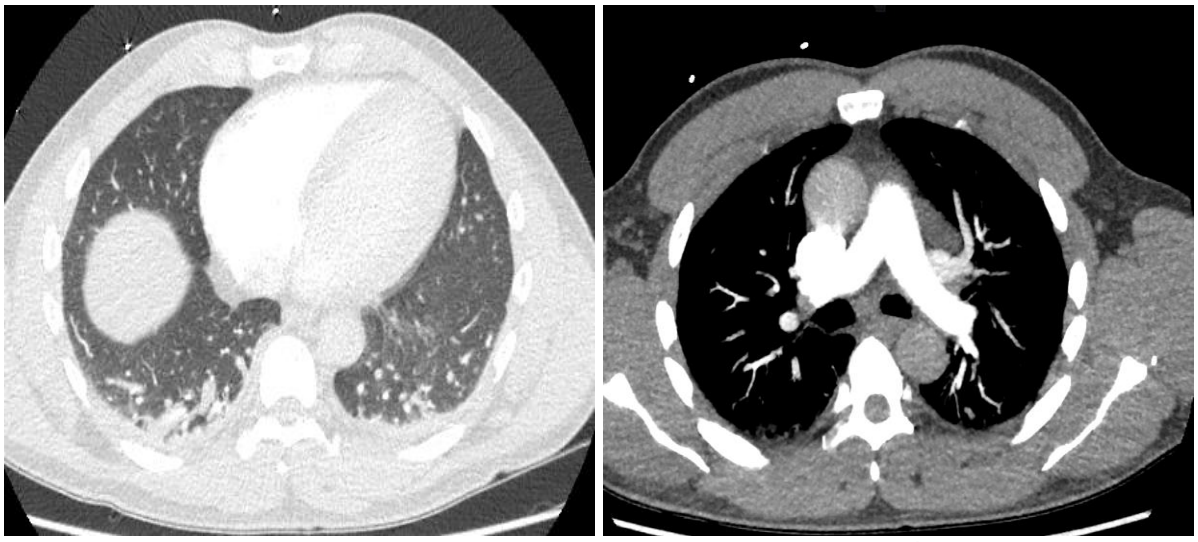
CTPA is more sensitive for imaging atelectasis than a chest x-ray. It can help identify the cause and type of atelectasis; for example, it may show lung mass, pleural malignancy or effusion with pleural effusion. It is also useful in patients with moderate atelectasis or associated with consolidation.

As in the figure below, the chest x-ray is inadequate to diagnose small to moderate atelectasis. In this case, CTPA in figure 4.23 confirms moderate basal atelectasis, which the x-ray could not detect.



a b

figure 4. 9: X-rays lungs seems to be clear (a,b). However, same day CTPA in figure 4.23 confirms moderate basal atelectasis, which is the cause of chest pain and hypoxia.



a b

Figure 4. 10: Low dose CTPA (b), (a) with moderate atelectasis in the patient presented with chest pain, SOB, chest pain and hypoxia for the last few days.

Low dose CTPA in figure 4.24 is adequate to examine atelectasis and helps determine what contributes to atelectasis, such as mucus plugs, bronchogenic carcinoma, or foreign bodies. A chest x-ray in these situations is often inadequate or inconclusive; low dose CT helps identify the cause and the distinction between obstructive or compressive atelectasis.

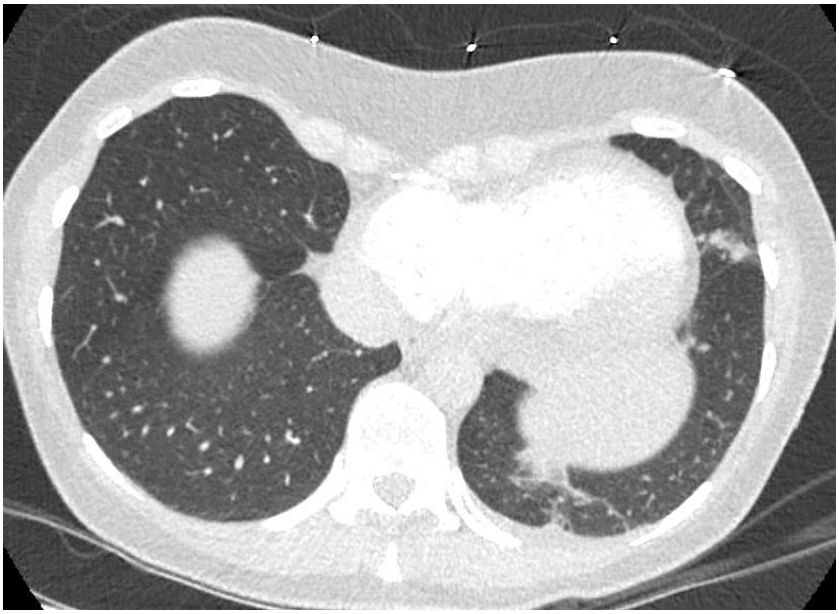


Figure 4. 11: Minor atelectasis in the left lower lobe.

4.1.3.7.2: Severity of Atelectasis

The severity of the atelectasis is a function of the size of the lung tissues involved. Atelectasis which impacts a small area, may not result in significant symptoms since the large part of the lung may offer adequate oxygenation. Nevertheless, where a large lung area is affected, the patient may not receive adequate oxygenation. Therefore the patient may experience dyspnoea. Atelectasis may also result in pneumonia distal to the obstruction.

Generally, atelectasis is not a severe condition, but where there is an underlying malignancy, or a large lung area is affected, this reduces lung effectiveness and can be life-threatening.

The treatment of atelectasis involves treating the underlying cause, which has often been diagnosed on CT. The intervention relies on the cause of the atelectasis; for example, bronchial cancer may involve the elimination of a tumour; in this case, operation, stent, chemotherapy, and radiation therapy may be required. Where the contributor is mucus, then bronchoscopy with an air pulse vibrator or mucus clearing apparatus mat be utilized to

remove the mucus plugs. Additionally, supplemental oxygen may be used to relieve shortness of breathing[220].

In Summary, other uncommon differential diagnoses reported in the retrospective review were pleural effusion, pulmonary oedema, aortic dissection, pneumothorax, lung masses, bronchiectasis, rib fractures, asbestosis, pulmonary hypertension, lymphangitic carcinomatosis, pulmonary fibrosis, pericardial effusions, mesothelioma and myeloma. These are not discussed as they were uncommon findings.

It is essential to know that it is often difficult to differentiate between acute respiratory conditions and PE; sometimes, clinicians can initially make a wrong diagnosis. Even those who follow best practice guidelines will have challenges in differentiating PE from the above conditions. However, good history and physical examination, assessment of pretest probability, possibly arterial blood gas, pulse oximetry, D-dimer test, and chest x-ray can decrease increasing CTPA referrals.

This retrospective review on CT pulmonary angiogram exams demonstrated a larger list of differential diagnoses and incidental findings. To further understand the alternative or differential diagnosis of chest pain, a survey of emergency medical doctors at this facility was undertaken to examine their views on PE differential or an alternative diagnosis when assessing pulmonary embolism.

4.2: Section Two: Questionnaires of Medical Doctors Regarding PE Differential or Alternative Diagnosis

4.2.1: Method

Senior emergency medical doctors (registrars and consultants) were consulted in unstructured interviews to identify their opinions regarding the differential diagnosis or alternative diagnoses they consider when assessing pulmonary embolus or chest pain and dyspnoea.

Questionnaires were formulated after an unstructured interview with emergency medicine consultants, the questions were prepared, then consultants then had further input, and the modified questions were presented as a questionnaire. In the questionnaire, medical doctors were asked to rank order the seven most common alternative diagnoses or differential diagnoses that they thought caused pleuritic chest pain and dyspnea. The questionnaire is presented in appendix 1.

The involvement of senior emergency medical doctors was voluntary. A sizable number, 40 in total, of doctors in the emergency department hospital were chosen; of these 31 doctors returned the questionnaire. The doctors were assured of anonymous responses to the survey in order to ensure honest and truthful answers with reduced bias. Questionnaires were distributed in hard copies. Some doctors did not fully respond to the questions; hence, only questions fully completed were utilized in the analysis.

4.2.2: Findings

The views of emergency medical doctors regarding the differential diagnosis of chest pain and dyspnoea were ascertained. The main alternative or differential diagnoses for chest pain for doctors at this facility were: Pneumonia, COPD exacerbation, acute asthma exacerbations and pneumothorax. The main alternative or differential diagnoses for dyspnoea for doctors at this facility were: COPD, asthma exacerbation, pneumonia and pneumothorax. This is presented in ranking order one to seven in tables 4.2 and 4.3).

Compared with the information obtained by the retrospective review, there are agreements that pneumonia and COPD exacerbation were both the major causes of chest pain and dyspnoea and expected alternative/differential diagnoses for chest pain and dyspnoea. However, while asthma exacerbation and pneumothorax were rated as the common alternative diagnosis in the medical doctor's questionnaire, only one pneumothorax

was found in 748 CTPA examinations. No single asthma case was noted in the retrospective review. The latter is most likely accounted for because it is a clinical diagnosis and finding for it on CTPA is unlikely or non-specific.

Table 4. 3: Response ranking for alternative diagnosis that causes pleuritic chest pain.

Diseases	**Number of responses raking(1 to 7)**						
	Raking 1	Raking 2	Raking 3	Raking 4	Raking 5	Raking 6	Raking 7
Pneumonia	19	5	2				
COPD/Emphysema		10	5				
Pneumothorax		10	6	2	1		
Aortic dissection				5	6	3	
Asthma	7	9	2	7	2		
Acute coronary syndrome		1	6	7	6	9	7
Lung cancer			1		4	2	5
Pulmonary hypertension				5	8	2	1
Costochondritis		2		7	2	4	
Pericarditis and myopericarditis		2	6		1	2	1
Atelectasis	1		4			5	
Rib fracture			5	3	2		
Fibrosis					3		2
Bronchiectasis					3		2
Other(Pleurisy)		1					

*Some doctors did not fully respond to the questions.

Table 4. 4: Response ranking for alternative diagnosis to PE that causes dyspnea.

Diseases	**Number of responses raking(1 to 7)**						
	Raking 1	Raking 2	Raking 3	Raking 4	Raking 5	Raking 6	Raking 7
COPD emphysema	12	3	8	2			
Asthma	8	14	3	3			
Pneumonia	6	4	2	6	1	2	2
Influenza	1	2	1		11	1	1
Pneumothorax	4	4	3		3	1	
Acute coronary syndrome				1	1	4	2
Congestive heart failure	2	1	5	2	2	4	1
Atelectasis	1						7
Pericardial effusion				3			
Lung/bronchi cancer					1	3	
Interstitial lung diseases			1				
Panic attack						2	1
Rib fracture							1
Other							

*Some doctors did not fully respond to the questions.

4.2.3: Discussion

In the retrospective review and medical doctor's survey, the main alternative or differential diagnoses for chest pain and dyspnoea were pneumonia and COPD exacerbation. Although acute asthma exacerbations were indicated as alternative or differential diagnoses for chest pain and dyspnoea in the doctor's survey, they were uncommon in the retrospective review. However, the clinical presentation of some patients who had CTPA showed recent exacerbation of asthma. There are several reasons why asthma is cited by doctors as differential diagnosis but not seen on CTPA, this is discussed below.

Asthma exacerbation can show clinical presentations similar to PE, such as chest tightness and sudden breathlessness. This is because the airways become filled with thickened mucous, and themselves become swollen and inflamed and ultimately constricted because of excess production of mucus and inflammation in the bronchial wall.

The above inflammation can cause asthma exacerbation, which is reversible airway obstruction. A number of recent studies have reported an association between the above asthma exacerbation and acute pulmonary embolism[221-224]. What is the clinical presentation that is more common in asthma than PE?

Asthma is very similar to COPD; the patient will have a history of asthma. The condition gets better with bronchodilator and steroid medications, with bronchodilator reversibility (often >15% improvement in FEV1 and at least 200mls post-bronchodilator). Specific triggers include dust or dust mite allergies, cold weather, pollen/grasses, animal dander/furs, perfumes, exercise-induced and often viral URTI infections. Patients clinically often have a wheeze and cough (often non-productive or occasionally productive of mucoid sputum). Patients often have tachypnea, increased work of breathing and tachycardia during asthma exacerbations. In severe asthma exacerbations, they may have desaturation or Type 2 respiratory failure on the arterial blood gas. Often patients complain of wheeze with central chest tightness, but they do not get haemoptysis or pleurisy. Often there is no fever unless the asthma was triggered by a viral or bacterial URTI or chest infection[225, 226,174].

An exacerbation can pass quicker than with COPD. But it can also last for many hours/days like COPD.

In some instances, a chest x-ray is normal, particularly in the initial days of the ailment. Chronic asthma is linked with hyperinflation, inflammation- thickening of the bronchial wall, diaphragm flatting, peripheral vascular markings' and increased lung volume (figure 4.12).

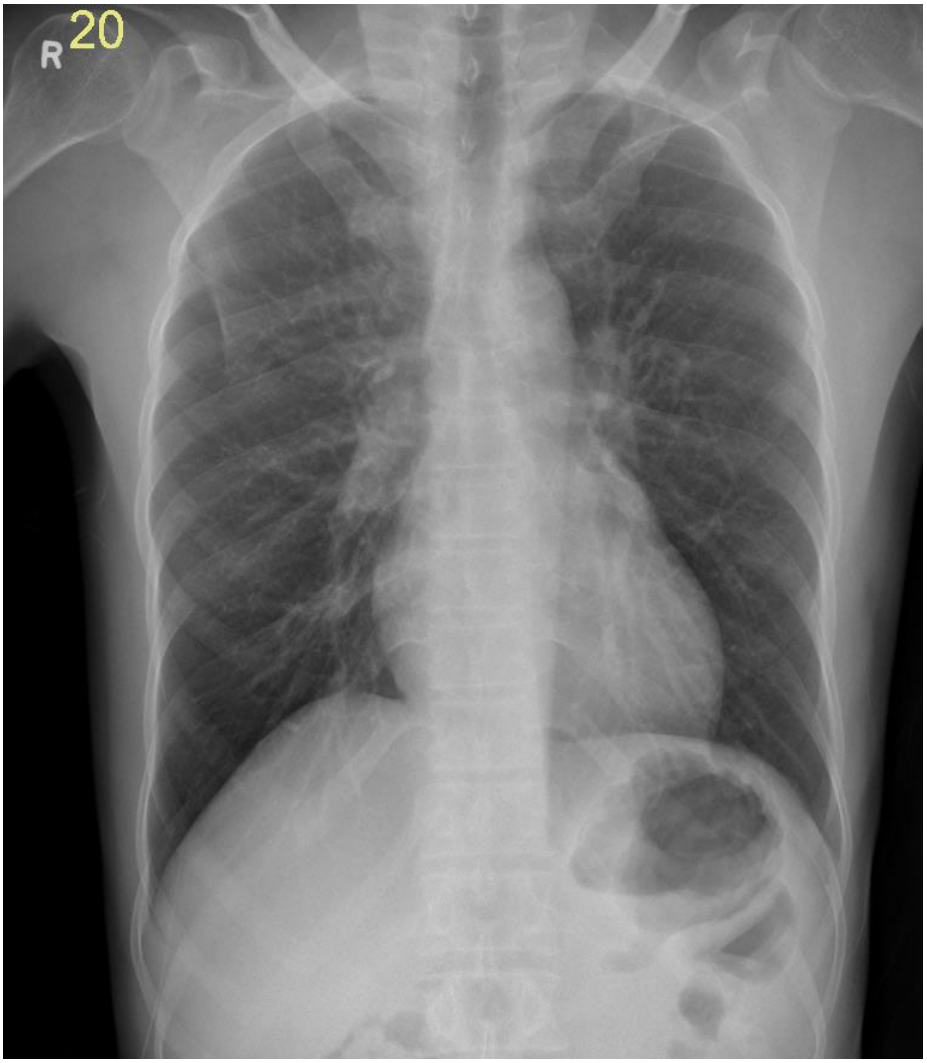


Figure 4. 12: Patients presented with asthma and flulike sickness with crackles lung basis.

Knowing patients' history is crucial in differentiating asthma or COPD from PE. Some of the commonly prescribed drugs to patients with asthma or COPD include bronchodilators and corticosteroids. They should be allowed to work prior to recommending the patients to undertake CTPA.

It is also important to know one-fifth of the patients who presented with asthma exacerbation who had CTPA had a positive pulmonary embolism. Hence it is also is essential not to overlook PE in patients with other comorbidities[224 182, 220, 319].

In summary, it should be noted even though the views of emergency medicine physicians regarding the differential diagnosis of chest pain and dyspnoea were an important. However, the retrospective review is more reliable than the survey of emergency medicine physicians regarding the differential diagnosis of chest pain and dyspnoea.

These findings are essential in designing a new protocol that can address the above issues. The next section discusses a survey and qualitative assessment given to doctors to assess the reasons behind physicians' overutilisation of CTPA and proposes methods to decrease this trend.

4.3: Section Three: Factors Contributing to CTPA Overuse

4.3.1: Aim

To determine the main contributors and issues leading to CT pulmonary angiogram overuse and outline recommendations to decrease unnecessary CTPA examinations.

4.3.2: Introduction

CT pulmonary angiogram has widespread availability in the emergency departments, it has fast image acquisition with little preparation required, and it also has high diagnostic accuracy. However, there is overuse in CTPA. Imaging referrals from medical doctors can be inappropriate:

- When no imaging is indicated due to low risk. for PE. (e.g. Wells score <2 and negative D-dimer).
- When imaging is indicated, but incorrect modality or protocol nevertheless is chosen (e.g. symptoms are due to acute respiratory diseases which chest x-ray is sufficient to diagnose, such as pneumonia or pneumothorax)
- When the timing of imaging is incorrect, for instance, image requests too early before accurate assessment[227].(patients dyspnoea due to asthma or COPD get CTPA too early)

This raises concerns about increased radiation exposure to patients. It is recognized that radiation exposure is linked to the possibility of developing cancers, particularly among pregnant and young patients.

Increased health care expenses such as overheads, maintenance, and cost of staffing are other concerns. The average cost of a CT pulmonary angiogram is approximately $450 in this department; this is considerably greater than non-contrast CT scans. This further increases Medicare associated diagnostic imaging expenses, which already cost more than $3.5 billion annually in Australia[227]

On retrospective review, the positive rate for PE was 11% in 2019; however, in the validation of the protocol validity and reliability section demonstrated positive rates of less than 10%. According to other research, a positive rate of 10 % or less reflects CTPA overuse, where the CTPA becomes a screening test rather than a diagnostic test [11, 130]. Therefore it is essential to discover the underlying issues of why patients were having more CTPAs.

4.3.3: Method

Senior medical doctors were consulted in unstructured interviews to identify the issues with regards to over-ordering; questionnaires were formulated after the unstructured interview with emergency medicine consultants. After the initial interviews, questionnaires were prepared, the original senior medical doctors then had further input and the modified questions. The final questionnaires were presented to hospital clinicians. Involvement was voluntary. A sample size comprised of 63 physicians was obtained, including intensive care doctors, general surgeons, radiologists, and emergency doctors. The surveys were given to doctors, and the survey was designed along the Likert scale lines and shown in appendix II.

4.3.4: Findings

The Survey found that over 75% of the participants believed that non-specific PE signs and symptoms or similarities between it and various types of acute respiratory ailments were the main contributors to CTPA overuse. This stood as the most common response among the respondents; 45 out of the 63 medical doctors acknowledged similarities among the symptoms were the main contributors to CT overuse. It was also found that other factors, which led to CT overuse, comprised a lack of experience in some junior physicians and doctors' fear of a lawsuit, as shown in table 4.5.

Conversely, most physicians held that the most appropriate strategy of decreasing CTPA overuse is utilising D-dimer testing alongside a probability tool such as the Wells score prior to CTPA assessment. This is represented in table 4.6.

Table 4. 5: Physicians answers on factors that result in CTPA overuse.

No		Strongly agree	Agree	Neither agree nor disagree	disagree	Strongly disagree
1	Symptoms are similar to other acute respiratory diseases	4	41	2	15	1
2	Health providers fear a lawsuit	4	32	5	1	21
3	Lack of experience/radiation awareness in junior doctors	2	30		6	25
4	There is a lack of regulation in CTPA use	2	20	11		30
5	Doctors are unaware of the risk of radiation dose	1	10	2	9	41
6	Uninformed patients	2	15	4	2	40

Table 4. 6: Physician's answers on strategies to decrease CTPA overuse.

No		Strongly agree	Agree	Neither agree nor disagree	disagree	Strongly disagree
1	D-dimer/probability testing such as Wells score reduces CTPA overuse	3	45	5		10
2	Educating doctors about the risk of radiation may reduce CTPA overuse.	3	27	1	30	2
3	Educating patients about the risk of radiation may reduce CTPA overuse	1	23	7	31	1

The doctor's survey revealed a key issue that causes CT overuse and most appropriate strategy of decreasing CTPA overuse. These findings are essential for department audits and implementing policies that can reduce CT overuse.

4.3.5: Discussion

Signs and Symptoms Factors

This study identified that the most common for CTPA over-ordering was that belief that there is significant overlap between the signs and symptoms of PE and other acute respiratory diseases; for example, dyspnoea and chest pain are not specific and may be visible in various acute respiratory ailments such as pneumothorax, atelectasis, pleural effusion, emphysema and pneumonia. Therefore the clinical diagnosis of PE remains challenging for the doctors interviewed.

In this chapter's retrospective review, only 82 out of 748 cases were discovered to have a pulmonary embolism. However, 251 patients had an alternative diagnosis to explain the presentation, such as atelectasis, acute exacerbation of COPD and pneumonia. PE's

symptoms were similar to other respiratory ailments, which made it challenging for doctors to distinguish PE from different types of respiratory diseases.

4.3.5.1: Fear of Missing a Low-probability Diagnosis Factors

The second most important reason for CT overuse is the fear of missing a low probability PE which occasionally can lead to medical negligence and breach of duty of care. Over 50% of 32 out of 56 doctors surveyed physicians agreed or acknowledged that healthcare provider/medical practitioners' fear of a lawsuit stood as the second significant factor leading to CT overuse. CTPA examinations are then used partially as a defence against a lawsuit, not necessarily as an actual medical necessity.

One of the CTPA use reasons is to confirm PE diagnosis before treatment; this is because an anticoagulant medication utilised for managing PE is also linked with considerable bleeding risks and some mortality. Therefore an accurate diagnosis is necessary before treating patients. A consultant or senior doctor with broad experience is needed to identify patients who require or do not require CTPA and/or treatment. In the absence of having competent clinicians, junior doctors may continue undertaking defensive medicine with its attendant extra cost and risks. Unfortunately, this activity also results in increased radiation exposure among patients and further increases Medicare associated diagnostic imaging expenses, which is the wastage of valuable resources.

4.3.5.2: Absence of Regulation in CT Examinations Factors

In this research project, the absence and unpredictability of regulations were revealed as some of the problems that encouraged the overuse of CTPA, according to 20 out of 56 respondents in this survey. Besides, there is a broad range of inconsistencies among CTPA dose products, where some are associated with increased radiation exposure. Furthermore, there is a discrepancy in the physician's practice, and there lacks a precise cut politic to identify those who require CTPA. Therefore, clinical opinions differ among physicians and depend on their knowledge, experience, and skills. Therefore, better guidelines on which patients need or do not require CTPA and strict regulations preventing the quantity of radiation exposure to patients are necessary.

4.3.5.3: Patient Education Factors

Unfortunately, most patients remain uninformed about the radiation dose they receive from a CT examination. It was discovered among 70 respondents that most of them were lacking in basic knowledge of the quantity of radiation they acquired during a CTPA

assessment since only five were able to recall the estimated dose. This result is consistent with Caoili et al. (2009) research, which also revealed that 295 patients acknowledged little awareness about radiation dose regardless of achieving a high level of education since 51% of them had attained at least a university or higher education degree. They also found that most patients were unaware of the risk linked with CT scanning, as only 6% had knowledge that radiation linked with CT could increase the lifetime probability of cancer.

In an unstructured interview with emergency medical doctors, physicians were asked why most patients were not informed concerning the scan's possible risk and radiation dose. Those who commented on these issues revealed that their choice was wholly centred on the possible benefits in patient management, the threat of failure to have a scan, and the potential advantage of undertaking a scan overweighed the threat of exposure to radiation. Nevertheless, physicians also expressed that time limits and pressure from doctor to patient ratio influenced them in making decisions such as recommending CTPA for low probability risk patients.

4.3.5.4: Lack of Experience and Less Radiation Awareness Factors

Other factors of influence include little formal training on the radiation exposure subject during university and, therefore, physicians underestimating malignancy risk. Increasing radiation awareness is certainly required; this can be accomplished by performing teaching sessions and explicitly outlining the benefits of reducing radiation exposure to patients.

Besides, emergency physicians often fail to strictly adhere to hospital regulations, for example, D-dimer test, detailed history and physical examination and using a verified probability scoring system to assess the risk of PE. For instance, utilising the D-dimer test routinely allows patients, particularly with those patients low clinical suspicion for PE and a negative D-dimer level, to forego CTPA assessment.

The following review discusses how doctors often fail to adhere to the D-dimer test strictly.

4.3.5.5: What Percentage is the D-dimmer Test Used in this Hospital?

This retrospective review involved 200 participants with CTPA who were selected randomly from a Picture Archiving Communication System (PACS) and pathology archiving system. The main objective was to determine whether the emergency physicians were utilising a D-dimer test among patients, particularly in patients aged below 50 years. The

purpose of this study was to evaluate the proportion of CTPA that could possibly have been avoided by the use of D-dimer in patients presenting with suspected PE.

4.3.5.6: Findings

In this retrospective review, 200 patients with suspected PE who underwent a CTPA examination were identified over six months between April 2019 and November 2019. Among this group of patients, 15 PE or positive results were identified. 55% of the patients underwent CTPA in the absence of a D-dimer test being conducted. Out of the 200 patients, 24 patients were aged 50 years or less and had no D-dimer test, and 39 patients' age 50 years or less had D dime before CTPA.

31 of the patients who were aged 50 years or less had undergone a D-dimer test which was increased but less than 1 mg/L; out of the 31 patients, only one patient was positive for PE on CTPA, as illustrated in table 4.7.

Table 4. 7: Retrospective review, 200 patients with suspected PE, the percentage with D-dimer test.

Clinical scenario	Number of patients (n=200)
D-dimer not taken	111
Under 50 years old without D-dimer	24
Under 50 years old with D-dimer <1 mg/L	31
Under 50 years old with D-dimer >1 mg/L	8
All patients with D-dimer <1 mg/L	55

The results of this research project reveal that some conditions besides PE results in increased D-dimer levels. They comprise of increased age, atelectasis, consolidation, neoplasia, inflammation and infection

4.3.5.7: Emergency Doctor's Questionnaire

Thirty-one emergency physicians were questioned at which level an increased D-dimer warrants CTPA amongst PE suspected patients. Their responses are visually demonstrated in figure 4.13.

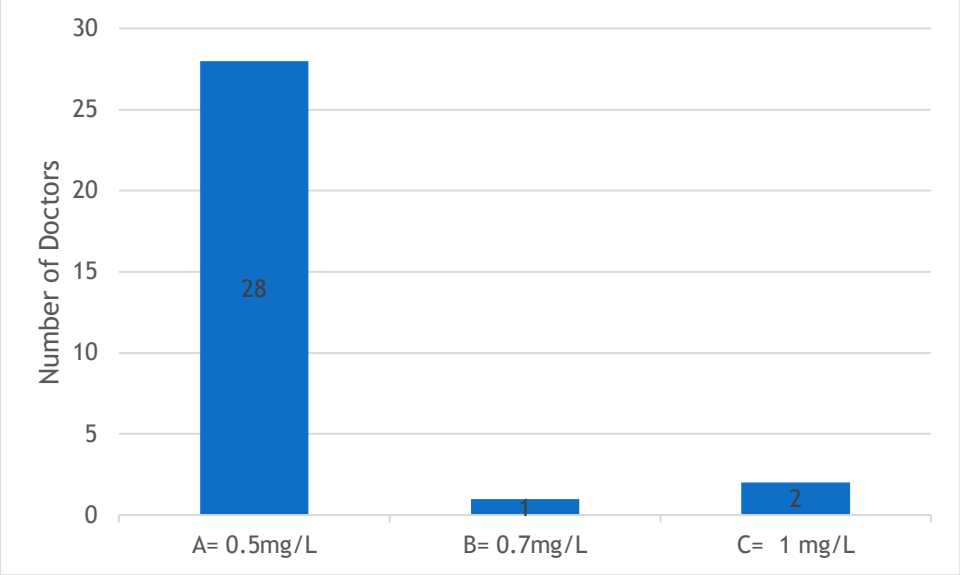


Figure 4. 13: Doctors' responses on D-dimer threshold to warrant CTPA.

The majority of the physicians questioned indicated when D-dimer is raised 0.5mg/L it warrants further imaging in those patients with suspected PE. However, this view's validity is questioned as the above retrospective review found that most patients with D-dimer <1mg/L had a negative PE.

Hence the common view amongst senior clinicians is that the D-dimer test should not be used in isolation. This is important as many conditions other than PE may result in increased D-dimer levels, such as increased age, neoplasia, inflammation, and infection all contribute to raised D-dimer levels. Thus, the findings should be explained in the context of clinical evaluation.

Patients with suspected PE should undergo probability testing, as is indicated in various literature. For example, the most current is Pulmonary Embolism Rule-out Criteria (PERC), such as Geneva score or Wells score. These scoring systems effectively guide emergency physicians to enhance their diagnostic methods as well as patient treatment.

Furthermore, PE suspected patients should recognise it is necessary to question doctors of the use of CTPA. For example, they should ask the quantity of radiation exposure they acquire from the assessment and if there are alternative radiation-free imaging modalities. CTPA emerges as the only imaging modality present, as is common in most medical imaging departments; a low dose protocol that uses low tube voltage with tube current modulation should be used.

To further reduced the radiation dose, CT scanning should be avoided where the referral is ambiguous, or the assessment would only result in radiation dose and fails to

answer the clinical questions. Furthermore, imaging teams should treat doctors to substitute with non-ionising modality when imaging is not fully justified. Other less ionising chest x-ray imaging should be used as initial imaging. It is sufficient to answer a clinical question, such as cases where symptoms overlap with differential diagnosis of pneumonia or pneumothorax.

In summary, doctors should be aware of the risks of radiation, and they should reduce the number of CTPA scans ordered as they are often not clinically indicated. Clinicians should also inform patients about the risk of CT examinations and should monitor patient exposure. Imaging staff conducting CT studies should use a protocol with reduced radiation dose as low as reasonably attainable.

Chapter 5: Strategies of Attaining Reduction in Radiation Dose:

This chapter contains four sections. Section one discusses the phantom test for tube voltage. Section two discusses the development of a low dose CTPA protocol. Section three discusses image quality and radiation dose for the improved 80kV CTPA protocol compared to the standard 100kV CTPA protocol. Section four discusses image quality qualitative testing with a survey of medical doctors.

Primary Objective of this chapter

This study's primary objective of this chapter is to design a new low-dose 80kV CTPA protocol with reduced image noise, which decreases radiation dose without compromising the image quality. To achieve the above objectives, this study will explore the following methods to reduce radiation dose: 1) Using low tube voltage of 80kV with tube current modulation; 2) Using an adjusted standard deviation of tube current; 3) Altering the reconstruction processing and algorithm-kernel to enhance image quality.

Utilising low tube voltage and image noise reduction techniques are thought to be the most direct techniques for obtaining a reduction in radiation dose whilst maintaining image quality. Table 5.1 and figure 5.1 illustrates the specifications of the CT scanner utilised during this research project.

Figure 5. 1: Toshiba Aquilion, one GENESIS Edition with detector 320 rows[228].

Table 5. 1: Specifications Toshiba Aquiline, one GENESIS main specifications.

Detector	**PURE Vision detector 320 rows, Rotation time Min. 0.275 s*1, 0.35 s**
CT gantry	Bore size 78 cm
	Bore depth 38.7 cm
	Tilt ± 30°
Patient Couch	Load 220 / 315 kg, 694 lbs*2
	Max. scan range 150–200 cm*2
CT Reconstruction speed	Volume 5 s
	Helical Max. 80 fps
Reconstruction	Iterative reconstruction AIDR 3D*3 Enhanced
	MBR
Installation	Power capacity 125 kVA*1, 100 kVA
	Space Min. 19 m2. (short couch), 204 ft2
Images and specification are adapted from (Canon Medical Systems 2020,) [228].	

5.1: Section One: Phantom Tests with Alternative Tube Voltages (kV)

5.1.1: Introduction

A phantom experiment was conducted to ensure that the study participants were not impacted negatively by exposure to radiation using the new protocol. This test was conducted in the medical imaging department on the same scanner that would be utilised for the remainder of the study. Quality checks were performed prior to undertaking low dose CTPA experiments, steps were illustrated in chapter one, end of section four.

This experiment examined radiation exposure when the kV is decreased to 100 kV from 120 kV after this kV was further reduced to 80 kV. The experiment also assessed the radiation dose saved with the reduction in tube voltage. This was an important experiment due to the differences among the previous studies on the extent of radiation reduction thought possible with lower tube voltage. It was essential to conduct a phantom test to determine the amount of radiation reduction possible after decreasing the tube voltage to 80kV.

5.1.2: Method

A phantom test analysis was attained by utilising a 32cm cylindrical phantom to measure the impact of low kV on the reduction of radiation dose and image noise. The research scanned the CT phantom ten times each by utilising 120, 100, and 80kVs. The experiments were conducted with a multi-detector 320 row Toshiba Aquilion One CT Genesis edition in the absence of the radiation reduction software known as forward projected model-based Iterative Reconstruction Solution (FIRST). All CT scanning parameters were kept unchanged; only the tube voltage setting was adjusted from 120 to 100 and then to 80kV. Dose length produced was measured in each set of images from the CT dose results.

5.1.3: Results

5.1.3.1: Radiation Exposure and Dose

A significant variation was noted in the dose length product and the effective dose between the 120, 100, and 80kVs tube voltages. Mean dose length products were 34.8, 20 and 9.2 Gycm at 120, 100 and 80kV, respectively.

The mean DLP was markedly reduced in the lower tube voltage of 80kV compared to both the 120kV and 100kV; this is visually demonstrated in figure 5.2.

Furthermore, utilising the chest K-factor calculation, the mean effective dose of 80kV was noted to be 0.13mSv, which is 50% lower than the standard protocol mean effective dose of 0.28mSv at 100kV.

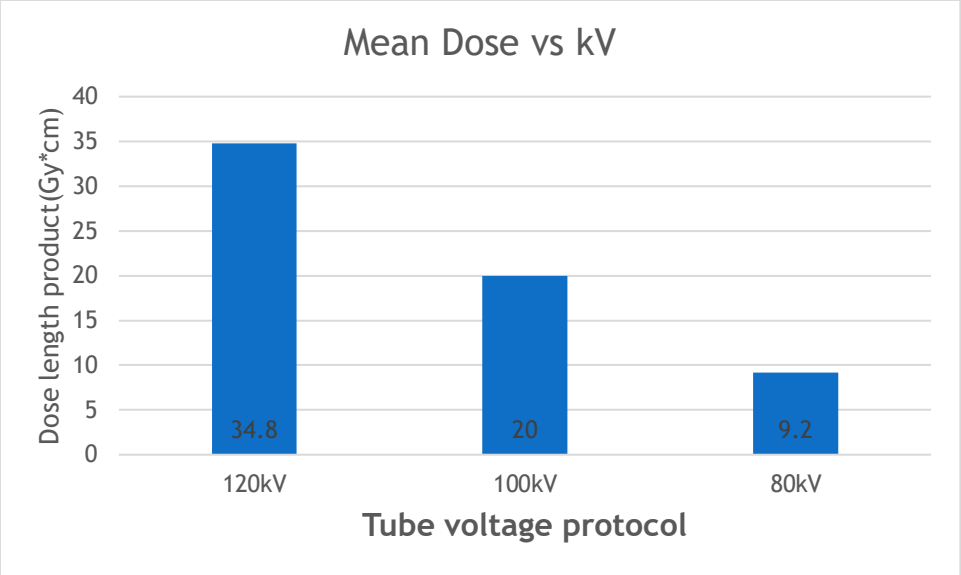


Figure 5. 2: The mean dose is decreased by 54% when a lower 80kV is utilised.

The above figure shows a major difference in the length product; this means 80kVs tube voltage can be a good technique if image noise is preserved.

5.1.3.2: Image Noise

The experiment's findings revealed that adjusting the tube voltage from 100kV to 80kV increased the imaging noise considerably. The standard deviation of the noise value at the centre of the phantom increased from 17.2 to 21.9 to 38.8 when going from 120 kV to 100kV to 80kV, respectively. Image noise is an undesirable fluctuation of pixels value in the image and can be recognised as a grainy appearance. It is caused by a combination of many factors such as quantum noise or quantum mottle, which in this case, is due to the insufficient number of photons. The number of x-ray photons detected per pixel is also referred to as a signal to noise ratio(SNR)[163]. Image noise is measured by taking the mean and standard deviation in each selected region of interest (ROI). This is visually demonstrated in figure 5.3.

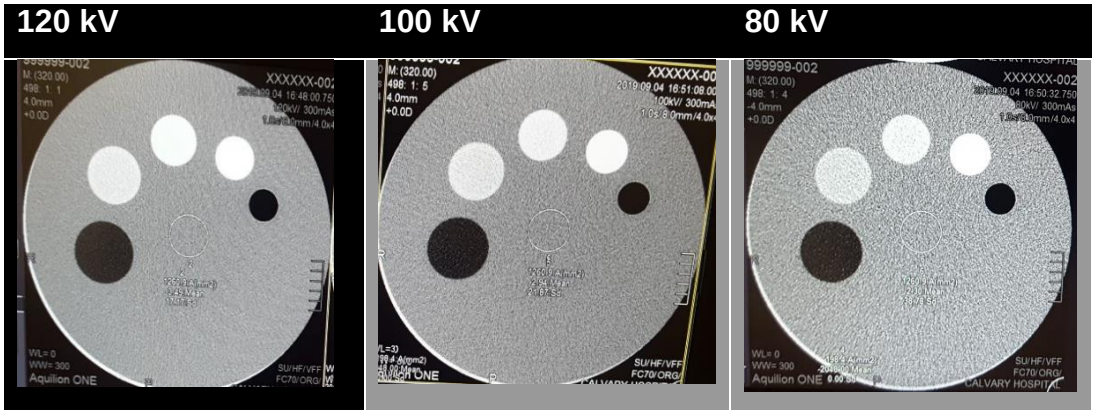


Figure 5. 3: Phantom image noise of the three tube voltage settings.

The standard deviation denoted by δ in the area of interest of the reconstructed image, is given by the formula below.

$$\delta = \sqrt{\frac{\sum_{i,j \in ROI}\left[f(i,j) - \bar{f}\right]^2}{N-1}}$$

Where i and j represent each pixel of a 2D image or region of interest, F represents the mean pixel density. N denotes the sum of the pixels on the image or within the region of interest ref 99. It is also possible to use a one-dimensional formula below.

$$Noise\ \sigma = \frac{\sqrt{\sum(x_1 - x_{mean})^2}}{(\mathrm{n}-1)}$$

x_1=individual pixel value

x_{mean}= average of all pixel values in ROI

n= total pixels in ROI (99)

5.1.4: Discussion

The phantom experiment provided a good indication that the radiation dose may be reduced significantly by decreasing the tube voltage; however, this came as a trade-off with increased imaging noise.

The image noise may be corrected by altering the scanning and image presentation techniques, such as altering the helical pitch, scanning time, slice thickness, reconstruction algorithms and tube current. Noise increases with small pixel size, thin slices, larger patient

size and lower tube voltage. Other factors that affect the image noise are the patient size and detector efficiency; these are unable to be altered due to influences on patient dose and image quality. The current research was focused on altering tube voltage to reduce radiation dose to patients; helical pitch, scanning time and slice thickness were not altered and therefore were not tested on phantom studies.

In most cases, there is a trade-off in various CTPA scanning techniques between radiation exposure and noise; this becomes significant when simultaneously trying to decrease radiation dose and enhance the images' quality. Therefore, further research and consultation with CT system engineers were conducted to minimise the effect of the image noise of CTPA with the lower tube voltage.

5.2: Section Two: Development of the New Low Dose CTPA Protocol at 80 kV

5.2.1.1: Aim

This research's primary purpose is to present the new low dose protocol, which decreases suboptimal images and radiation dose with imaging conducted on patients. The patient CTPA protocol was developed after the phantom study demonstrated a significant reduction in radiation dose with an 80kV protocol.

5.2.2: Technique

This research project used a 320-row multi-detector without the proprietary forward-project model-centred iterative reconstruction solution abbreviated as FIRST radiation reduction software. Patients were scanned with a low-dose CT pulmonary angiogram at 80kV with automatic exposure and current modulation, image reconstruction software process (proprietary name: AID 3D standard) and an effective mAs of 215. CT parameters are visually demonstrated in table 5.2. The reconstructions algorithm utilised a kernel FC 53, which was standard from the CT manufacturer.

Patients were scanned in a supine position; every examination was obtained with a single breath-hold. Craniocaudal scanning beginning from the lung apex to the costophrenic angles. Patients were given 40 - 70ml of IV contrast with an injection rate range of 4-5ml/sec. Bolus tracking was utilised at the level of the pulmonary trunk; a trigger of 180 HU and a 5 second delay time were used as per standard practice.

Ethics permission was obtained from the local Human Research Ethics Committee.

Table 5. 2: Low dose CTPA 80kV parameters.

	kV	mAs eff	Rotation	Pitch	Detector Collimation
Low dose	**80**	**215**	**0.37s**	**0.8**	**0.5 x 80**

5.2.2.1: Lower Tube Voltage Protocol Enrolment

As a first step, this study enrolled small size patients with suspected PE that needed CTPA for the 80kV protocol. These groups of patients often have less muscle and need less radiation penetration of the standard protocol. Also, smaller patients tend to have less image noise while the image quality is projected to be suitable with a lower tube voltage. Therefore

this study conducted a staged enrolment starting with patients less than 60kg and increasing by 5kg increments once imaging was evaluated and accepted at each stage by the head reporting radiologist. The 5kg increments are aimed to have some form of quality measure in place to protect image quality. The first patients scanned involved less than 60kg and had chest depth of less than 19cm (small). A chest depth may be described as a measurement taken in the front of the chest to the back and from the sternum to the spinal groove; this is visually demonstrated (line between A and B) in figure 5.4.

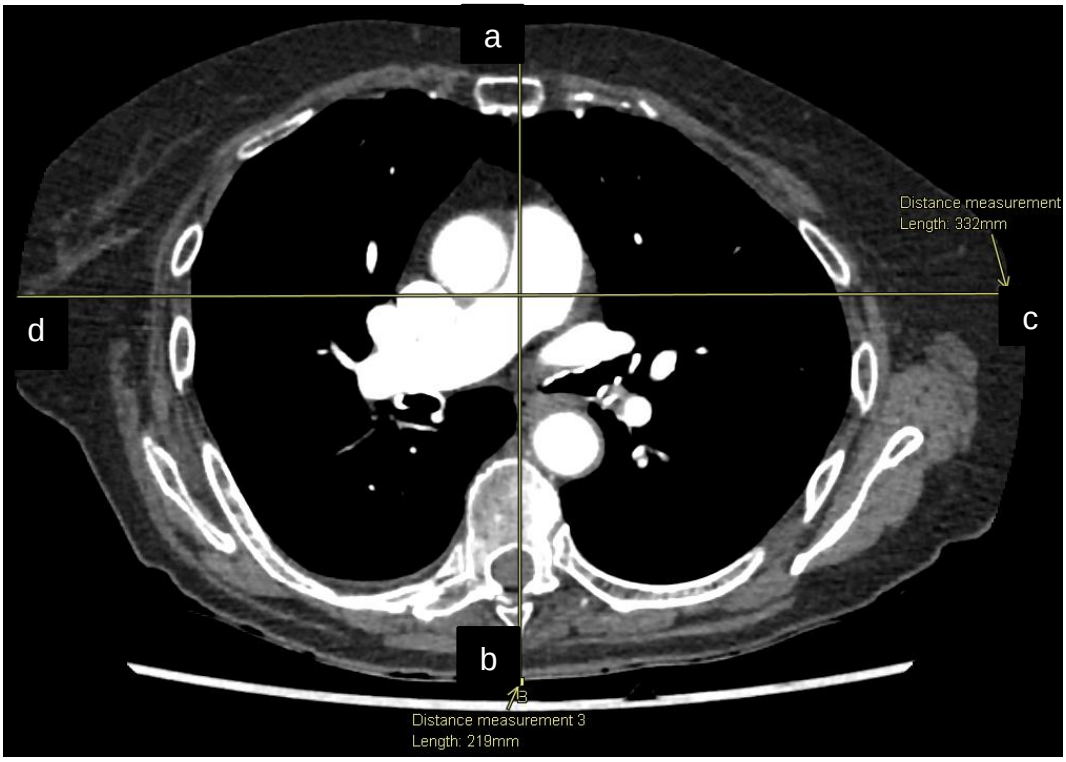


Figure 5. 4: Axial CT images visually demonstrating chest depth of 21.9 cm (the line between A and B).

Using a chest depth measurement taken in the front of the chest to the back and from the sternum to the spinal groove is more effective than using the only patient weight because some patients, although they are large, their chest depth are small. This means they can have a lower tube voltage.

5.2.3: Results

After images were submitted to the head reporting radiologist at the initial weight (<60kg) no discernible variation between the image obtained from a standard protocol and low dose protocol was identified. Subsequently, the enrolment weight was increased by a 5kg increment and ultimately reached the mean weight of 80kg at this facility. At 80kg, a mild

increase in image noise was reported; however, the increase was neither a significant diagnostic problem nor an obstacle to the research's diagnostic accuracy. While the images were able to exclude larger pulmonary emboli, there remained a possibility of being unable to exclude smaller or subsegmental pulmonary emboli. It was also thought that this might reduce confidence in diagnosing other lung diseases and overall confidence. The initial evaluation of this section was the purely subjective opinion of the two reporting radiologists.

5.2.4: Discussion

This experiment showed that individuals weighing below 80kg could at least take advantage of this process in the absence of reduced imaging quality. The low dose CTPA examination's image quality was considered standard protocol among patients who weighed below 80kg. The overall diagnostic confidence for PE, contrast resolution, spatial resolution, and image noise, as well as optional lung ailment, was rated by the head reporting radiologist as acceptable. The assessment has been a subjective opinion of the radiologists. For the purposes of demonstration, acceptable image noise was illustrated in figure 5.5.

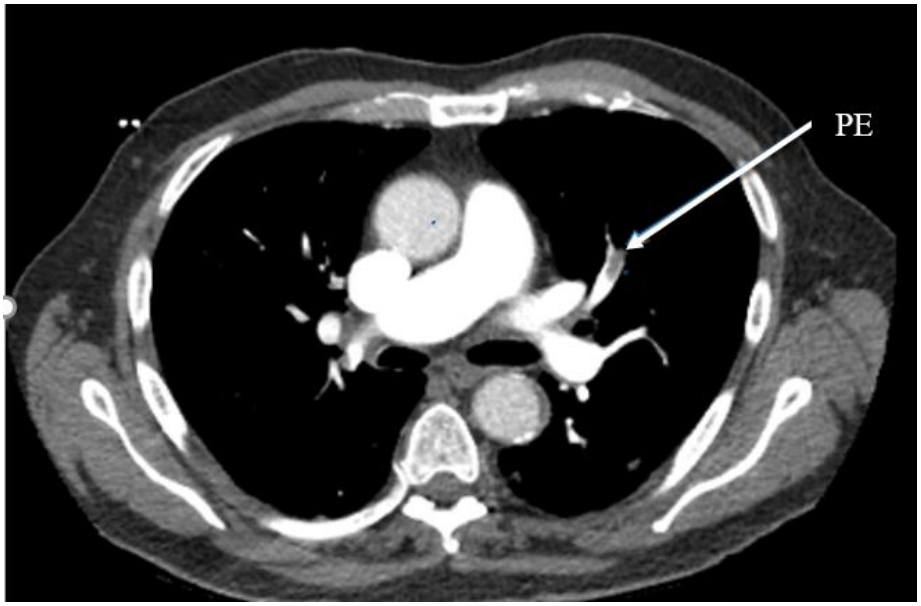


Figure 5. 5: Positive PE (arrow) with acceptable image noise, improved contrast enhancement and low radiation exposure of (0.95mSv).

The image quality of the low dose CTPA examination was considered to have adequate contrast resolution, and image noise is preserved in patients weighing below 80kg, as shown above, image.

5.2.4.1: Patients Weighing More than 80kg

Amongst patients weighing greater than 80kg, the image noise started to increase and was discernible by the reporting radiologists on initial subjective opinion. Conversely, the protocol's reliability and accuracy in diagnosing PE and its alternative or differential diagnosis were thought to be compromised by the image noise.

Previous research has long-established that image noise increased significantly in larger patients; this occurred in particular on the lung window as they accentuate higher frequency data, including noise. This reduces the general confidence in identifying other lung pathologies. Hence, image noise is required to be decreased to maintain image quality and diagnostic confidence.

5.2.5: Approaches to Reduce Image Noise

Image noise of CTPA images depends on photon detection, which is dependent on radiation exposure, slice thickness, patient size and detector efficiency. An effective method used to decrease image noise and maintain image quality is to increase tube current output slightly while using image noise reduction. For example, a method for achieving is to lower the standard deviation level, which automatically raises the tube current by a small margin; this is especially marked for larger patients. The image reconstruction process/algorithms reconstruction kernel was also adjusted while utilising lower kV protocols with tube-current modulation.

Image quality is a subjective notion which dependent on the purpose for which the image is acquired; however, any adjustment should consider the spatial resolution, contrast resolution, pixel noise, and resolution in the Z direction, slice sensitivity profiles and artefacts[229]

CT pulmonary angiogram image quality is directly related to its usefulness in providing an accurate diagnosis to either include or exclude pulmonary embolus or an alternative disease. European Image quality criteria stated while there is no internationally accepted definition of image quality, the degree of visibility is defined as follows:

Visualisation - organs and structures are detectable in the volume of investigation.

Critical reproduction- details of the anatomical structure are visible, clearly defined and sharp for specific indication can be differentiated to a level necessary for diagnosis for a particular disease in this case (PE)[230].

Overall, the true test of image quality is whether it serves the purpose of which it was acquired. It is, however, a common practice to express CT Image quality equation in terms of image noise with the following formula:

$$\sigma^2(\mu) = kT/(td^3R)$$

σ = variance resulting from image noise
k = conversion factor
T = transmissivity
t = slice thickness
d = pixel dimensions
R = exposure or radiation dose (99).

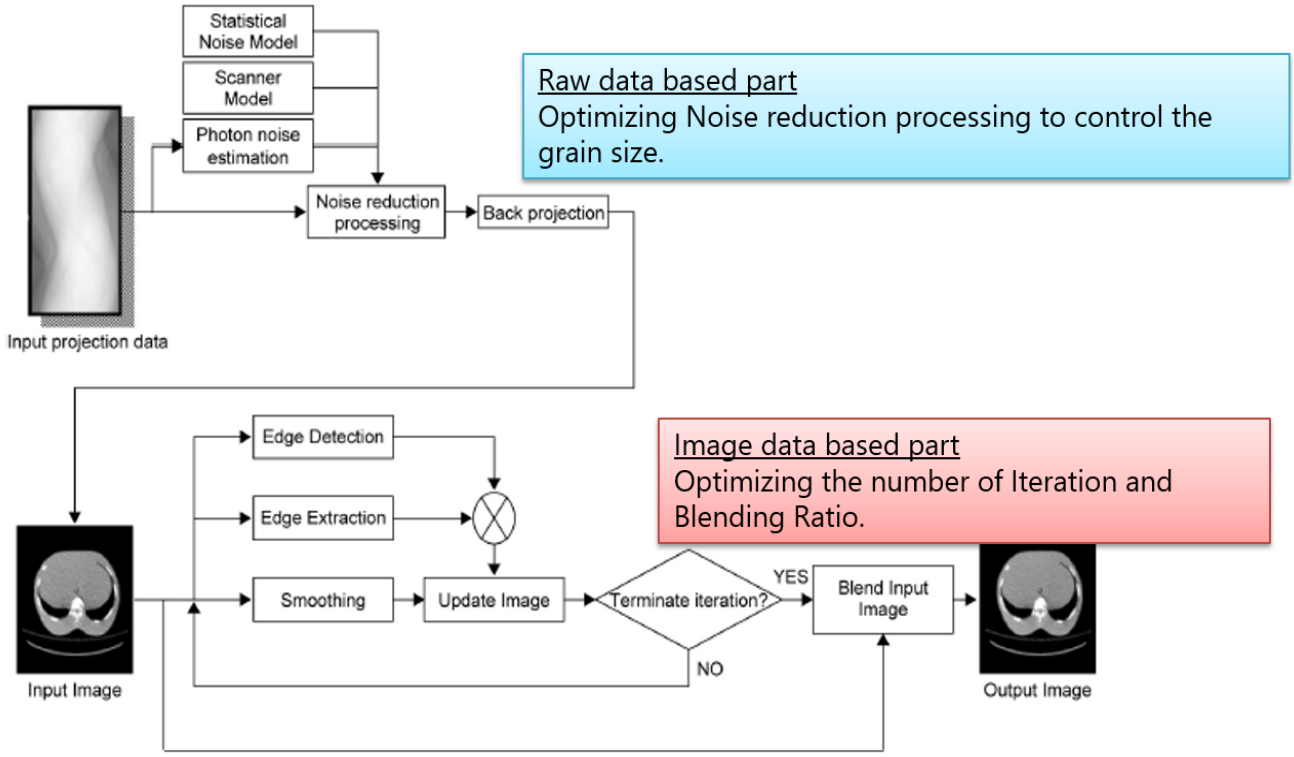
When discussing image quality, the major concern is how well do the CTPA images accurately represent the anatomy or pathology that has been scanned. Radiologists, in turn, are most concerned about the following two main features: high contrast resolution (commonly interpreted as the detail in an image or the ability to resolve two objects that are close to each other) and low contrast resolution (commonly interpreted as the accuracy of depicting density so that two objects can be easily differentiated based on their density). For instance, images with good high contrast resolution should be able to identify small emboli and images with low contrast resolution to differentiate embolus compared to artefact[163].

Nevertheless, reducing quantum noise, the grainy appearance caused by an insufficient number of photons is important while maintaining spatial and contrast resolution.

A number of other factors affect image quality, such as slice thickness, pitch, field of view, pixel size and reconstruction algorithms. However, the major factor affecting image quality and noise remains tube current, which directly influences the number of photons used to produce CT images, affecting the noise to signal ratio and contrast resolution. CT scanner used in this imaging department has a noise system to control grainy appearance on images; this is present in figure 5.6. However, further alteration is required in the 80kV protocol to maintain the signal to noise ratio.

Signal to noise ratio is an effective way to quantify the effectiveness of the protocol[231] and is defined as follows

$$SNR_{\lambda} = \frac{\left|\mu_{1-}\mu_{0}\right|}{\sqrt{\frac{1}{2}(\sigma\ \frac{2}{0} + \sigma\ \frac{2}{1}}}$$



Source: Personal communications: https://anz.medical.canon/[100]

Figure 5. 6: Noise reduction techniques available in the CT scanner[228].

The following sections discuss methods to increase tube current slightly so that quantum image noise is reduced whilst using a low kV.

5.2.6: Standard Deviation

Standard deviation (herein referred to as SD) describes the spread of data or dispersion of data. In the imaging quality domain, especially with considering noise, SD usually refers to the acceptable noise level. It is also known as the target SD set prior to acquiring imaging data. This is based on a reference level of image quality. SD is often expressed as:

$$\sigma = \sqrt{\frac{\sum(x_i - m)^2}{n - 1}}$$

x_i = data point
m = mean
n = number of elements

When considering imaging quality, the relationship between the standard deviation and noise is the following: Increasing the standard deviation level increases the image noise; it also reduces the mAs, whereas decreasing standard deviation reduces image noise and increases the mAs.

This study evaluated the SD levels and consulted Toshiba application engineers in the protocol development process, then changed from level 12 to level 8. Level 8 showed acceptable image noise with a decreased effective dose. Furthermore, level 8 accommodates most patients' size whilst maintaining image quality at 80 kV; overall, this protocol was found to reduce the radiation dose by more than a half.

The combination of lower SD level, 80kV with tube current modulation/sure exposure 3D (modulation the mAs in the X, Y, Z directions) attained the lowest level of radiation exposure necessary to achieve the target image quality. Tube current modulation accounted for changing patient size and also decreased the radiation dose whilst maintaining image quality. The tables below demonstrate the difference in effective dose when SD is altered alone. For the remainder of this study, an SD of level 8 was utilised. The initial and improved tube current setting is visually demonstrated in table 5.3 and table 5.4.

Table 5. 3: Initial pre-set for low dose protocol.

SD level	Maximum tube current setting (mAs)	Minimum (mAs)	Effective dose
12	500	80	215

Table 5. 4: Pe-set is changed to improve image quality.

SD level	Maximum tube current setting (mAs)	Minimum (mAs)	Effective dose
8	600	120	258

Clinicians and radiologists feedback was sought to assess the quality of images. The main findings that radiologists stated were that some image noise decreased among most patients scanned; however, there was still a minor increase in image noise in larger patients, however, for most image qualities are acceptable, as demonstrated in figure 5.7. Nevertheless, a slight escalation in radiation dose of around 8% is observed while using SD level 8 compared to SD level 12.

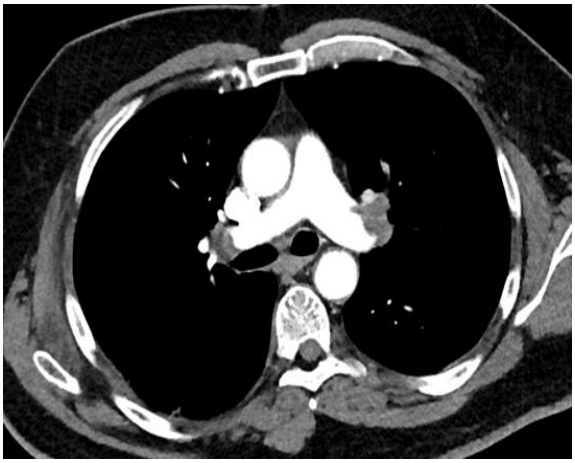


Figure 5. 7: An axial image with excellent contrast enhancement showing bilateral main pulmonary artery emboli.

When 80kV was utilised in the past, excessive noise involved a high SD level and low effective dose. This led to excess image noise that escalated exponentially with an increase in patient weight. Eventually, this resulted in most imaging departments ceasing the low dose protocols. In past CT systems, users were unaware of how to change the level of noise limit/optimise the protocol to suit their needs and for differing clinical examinations.

5.2.7: Algorithm Kernel and Image Reconstructions Process

The aim of this investigation was to further decrease image noise by using different imaging reconstruction algorithms. Several algorithms kernels were available for the Toshiba CT systems were explored to overcome the issue of image noise; these include Toshiba FC 50, 51, 52, and 53. The kernels available in this CT scanner system are described as smooth, standard and sharp. The higher the FC number (i.e. 52, 53, etc.), the sharper the image produced, the kernel accentuated differences between adjacent pixels. When producing sharper images, the tradeoff is that more mAs are required to produce less noisy images. Smoother reconstruction kernels remove image noise and artefacts by reducing differences between adjacent pixels. This is useful in reducing image noise but with the cost of reducing spatial resolution. Hence to reduce image noise while maintaining spatial resolution, an FC51 reconstruction kernel was chosen. This improved the definition of structures by emphasising the display of lung parenchyma, soft tissue and blood vessels. FC 53 algorithm kernels are better when looking at interstitial lung diseases, whereas FC51 algorithms appear to perform well in situations with high image noise, such as low radiation dose CTPA scans.

Image reconstruction processing applies noise reduction filters to enhance image quality; this is achieved by using a repetitive cycle of modifying spatial data frequency and thereby removing quantum image noise. This change was done within spatial resolution parameters, keeping an acceptable contrast to noise ratio and spatial resolution.

Concurrent to changing the algorithm kernel, the image reconstruction processing noise filter AID 3D *standard* was changed to AID 3D *strong* to decrease image noise further. The AID 3D *strong* decreased image noise on lungs windows, particularly when compared to the AID 3D *standard* when utilising the standard CTPA protocol.

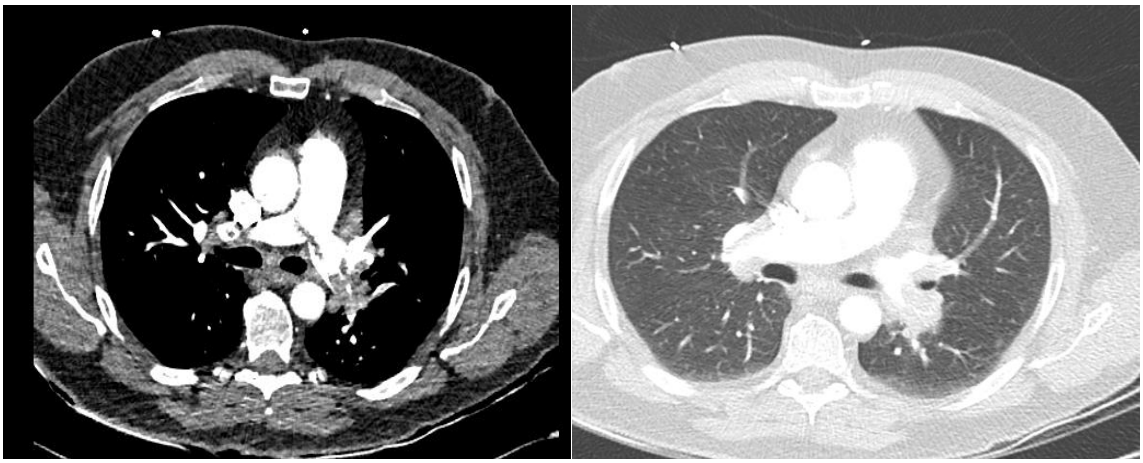
Furthermore, Sure Exposure 3D, the Toshiba proprietary automatic exposure control, was utilised alongside the adjusted reconstruction algorithm-kernel and image reconstruction process, kV selection, and standard deviation SD level 8 the desired noise level with acceptable radiation exposure. Sure exposure 3D modulates dose exposed within the X, Y, and Z paths according to the individual's body size. Sure exposure works with target SD level while considering slice thickness, tube current, image filters, and algorithms. In this technique, exposure can be reduced significantly while retaining the quality within the desired image noise. With a selection of low tube voltage Sure, Exposure 3D has shown an opportunity to decrease radiation exposure to different patients' sizes while obtaining diagnostic images of excellent image quality, as illustrated in figure 5.9 with exposure of 0.95mSv.

To validate study technique, this study reconstructed 36 images of patients who had CTPAs with the standard reconstruction algorithm-kernel FC 53 with AID 3D *standard* and altered algorithm FC 51 and AID 3D *strong*. Radiologist's opinion was enquired regarding image quality and the ability to see small structures; furthermore, radiologists were asked about the ability to discern subtle density differences, acceptability of tissue contrast, spatial resolution, image noise and overall acceptability of the images.

The practice radiologists indicated FC 51 with AID 3D *strong* to provided less image noise; this change is essential when imaging larger patients. It enhanced the quality of the image compared to standard settings figure 5.9, (a). It was found that FC 51 kernels had less image noise than images reconstructed with standard kernel FC 53. In addition, the altered algorithm smoothened the image by reducing noise, as displayed in figure 5.8. Nine radiologists used a Likert scale to assess image quality; an agreement scale used to measure respondents included 'unsatisfied, neutral, satisfied, and very satisfied with image quality.

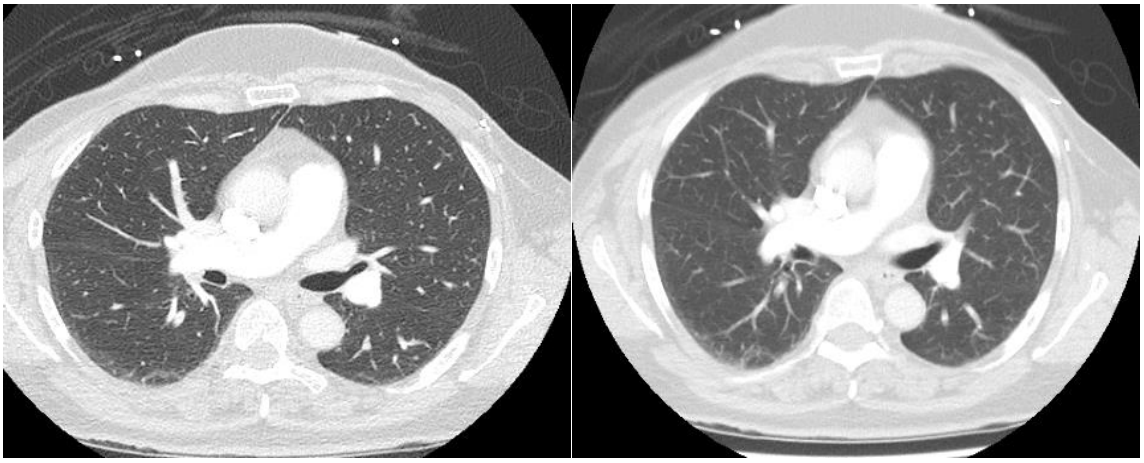
Image noise measurement in terms of signal-to-noise ratio (SNR) was performed by placing a region of interest (ROI) on the main pulmonary artery, paravertebral muscle on the right and left side and right and left upper lung lobes. The radiologist repeated each measurement three times at each location on the testing cases.

The FC51 was found to be more effective in decreasing image noise in the lung window for larger patients. Image quality and ways to improve for larger patients are discussed in chapter 6.



a b

Figure 5. 8: Image (a) extensive and marked bilateral pulmonary emboli. (b) Illustrates algorithm FC51 with AID 3D strong has lower image noise.



a b

Figure 5. 9: Image (a) original FC53, (b) altered algorithm with a smoothened image; it is often effective in reducing image noise.

The altered algorithm smoothened the image by decreasing noise; a contrast to noise ratio is also maintained, as shown above, image.

The contrast to noise ratio is calculated using attenuation pulmonary arteries and paravertebral muscle and divided by the standard deviation of paravertebral muscle[121].

CNR= $HU_{PA} - HU_{PM} / SD_{PM}$

When tested patients with similar size, image noise was slightly higher in 80kV patients, mainly lung window images; however, the increased image noise was not significant, and images were diagnostic to exclude PE and alternative diagnosis as illustrated in Figure 5.9, as per reporting radiologist[232]

In summary, it is possible to obtain the desired objective of reducing both the radiation dose and image noise while preserving the imaging quality. The following article one will compare image quality and radiation of the old or standard protocol to the new low dose CTPA protocol.

The following study intends to answer the question:

- Is the confidence in detecting pulmonary embolism at 80kV with improved image reconstructions processing, improved image reconstruction algorithm and adjusted standard deviation the same as a CTPA at 100kV?

5.3: Section Three: Prospective Comparative Study One: CT Pulmonary Angiogram with Reduced Radiation Exposure at Low Tube Kilovoltage

5.3.1: Abstract

This study's primary goal is to assess the image quality and radiation dose of the improved 80kV computed tomography pulmonary angiogram (CTPA) protocol compared to the standard 100kV CTPA protocol for the assessment of pulmonary embolism (PE). The study consisted of 100 patients who had clinically suspected pulmonary embolism and required a CTPA. Patients underwent imaging with a 320-row multi-detector Toshiba Aquilion One Genesis Edition in the absence of the proprietary radiation reduction software known as forward projected model-based Iterative Reconstruction Solution (commercial acronym 'FIRST'). Participants were divided into two groups: A and B. Group A was composed of 50 patients who were allocated to standard CT protocol using a 100 kV exposure setting and all other settings set as a standard by the manufacturer. Group B was composed of 50 patients who were allocated to a CTPA with an improved 80kV protocol, standard deviation level 8, an effective mAs of 258, reconstruction algorithm-kernel FC 51 within the lung window, and tube current modulation. A considerable decrease in radiation dose was observed with the low-dose CTPA protocol. The mean radiation dose was also decreased by 66% while using the improved 80kV protocol than when utilising a standard 100kV technique; this was achieved without compromising this study's diagnostic value. Furthermore, the contrast enhancement was considerably more significant, up to 40% higher when using improved 80kV protocol. The study found that a low tube voltage of 80kV CTPA protocol resulted in a considerable decrease in radiation dose and improved contrast enhancement without sacrificing the examinations' diagnostic utility.

Keywords: Image quality of 80kV; CT pulmonary angiogram; Low tube voltage; 80kV CTPA protocol; 100kV versus 80kV, Image quality and contrast enhancement assessment of 80kV.

5.3.2: Introduction

Pulmonary embolism (PE) is a possibly fatal disorder with persistent poor outcomes among hospitalized patients[233]. Most PEs emerge due to deep vein thrombus (DVT or blood clots) in the extremities, most often the legs and pelvis. The moment any thrombus is created, it may extricate, move to the inferior vena cava, eventually passing via the right ventricle in the pulmonary vasculature[2]. While most emboli are small and can be asymptomatic, occasionally, massive emboli can cause symptoms and may lead to death in 30% of the instances by damaging the right ventricular output[234, 235]. Thus patients with typical symptoms from PE should undergo timely diagnosis and urgent commencement of appropriate treatment[163].

CT pulmonary angiogram (CTPA) is often utilised, and it is an ideal imaging technique used for diagnosing PE. CT imaging, in most cases, has considerable advantages over other types of imaging modalities. For example, it has much more widespread availability, availability after hours, and fast image acquisition in the emergency department with little preparation required, and it also has high diagnostic accuracy. Besides PE, it can also show other diseases where pulmonary embolism is not the source of the symptoms, such as pneumonia or dissection. CTPA is also easy for physicians to interpret images once images are reconstructed. Such merits influence physicians to over-use CTPA, leading to 89% of surveys being negative. Over-utilisation of CTPA with high radiation doses raises concerns about increased radiation exposure to patients. It is recognised that radiation exposure is linked to the possibility of developing breast cancer, particularly among pregnant and young patients. Therefore, appropriate radiation dose reduction techniques are required in the absence of damaging the quality of the images, as a significant drop in radiation dose may result in diminished image quality and consequently missed PE and alternative diagnoses.

This study's main purpose is to present a novel low-dose CTPA protocol to ensure that radiation exposure is as low as realistically possible in the absence of affecting the image quality and diagnostic utility. Reducing radiation is possible by utilising different dose reduction methods, such as altering the reconstruction algorithm kernel, adjusting the standard deviation (SD), utilising low tube voltage (80 kV) with tube current modulation, and changing the image reconstruction process to improve image quality.

5.3.3: Material and Methods

The study involved 100 patients with suspected PE who required CTPA. Patients underwent imaging on a Toshiba 320-row multi-detector without the software for radiation reduction known as FIRST (commercial acronym). The study participants were categorised into Group A with standard CTPA protocol (control) and group B with the new, improved 80kV CTPA (test). Each of the control and test groups consisted of 25 women and 25 men patients. To ensure consistency, pair matching was conducted on the basis of similar age and weight distribution, as these are the most critical factors to control for radiation dose. Given ensuring similarity between the groups, the mean age of the participants in the control group, A, was 56.050±19.66 years, whereas, for the test group B, it was 54.06 ±21.52. The participants' mean weight in control group A was 69.88±14.23 kg, whereas for test group B, it was 68.96 ±13.45 kg.

Group A included 50 patients allocated to the standard CTPA 100kV procedure with reconstruction algorithm-kernel FC 53 with tube current modulation, the image reconstruction process AID 3D standard, and an effective mAs of 215. This data was gathered before implementing a low dose CT pulmonary angiogram protocol. Group B was allocated to low-dose CTPA with the image reconstruction process AID 3D strong, standard deviation setting of level 8 (Sure Exposure 3D), an effective mAs of 258, and 80 kV, as well as the reconstruction algorithm-kernel FC 51 in the lung window incorporated with tube current modulation.

All the imaging was obtained in a sole breath-hold and craniocaudal manner. The injection rate was similar between the patients; 40-70mL iodinated contrast medium (iopromide, commercial name Ultravist® Bayer pharmaceuticals) was administered with a 50mL saline flush. A minimum 18-G cannula within the cubital fossa was utilised with a 4.5mL/sec flow rate through a dual-headed injector. An automated bolus tracking system was formulated with a scanning trigger at 180HU and region of interest (ROI) positioned within the pulmonary trunk. ROI size was set at five mm^2. Two experienced radiologists with over eight years of experience reported the studies. The image quality of both groups was evaluated using a 3-point scale. For example, score 1: Images with no diagnostic issue and/or minimal noise (excellent image quality). Score 2: Images with no diagnostic problem but with minor increased image noise (good image quality). Score 3: Images with noticeable image quality issues and/or significant image noise (suboptimal image quality). In the case of disagreement on the scores, a consensus agreement was reached.

The study excluded patients under 18 years suffering from kidney failure with an estimated Glomerular Filtration Rate (eGFR<30) and chest depth greater than 30 cm or weighing over 105 kg. A region of interest was positioned at the pulmonary trunk to evaluate contrast enhancement, specifically to achieve the correct measurement in Hounsfield units (HU). Images that demonstrated contrast enhancement of more than 210 HU in the main pulmonary artery were accepted for having satisfactory contrast enhancement to detect PE[173]. The images were then ranked as suboptimal or non-diagnostic in cases where the contrast enhancement was lower than 210 HU in the main pulmonary artery or if the reporting radiologist graded the images as non-diagnostic or suboptimal. The radiologist provided the final assessment of imaging or diagnostic quality.

The data were presented in terms of statistical properties, such as minimum, mean, and maximum (with confidence interval) of radiation doses and contrast enhancement. The study presented the frequency distribution of the list of PE alternative or differential diagnoses.

The outcome variables, radiation dose, and contrast enhancement were measured using standard techniques. Side by side box plots was presented to visualise the differences and to show the distribution of the radiation dose and contrast enhancement

A hypothesis test was conducted to test if significant differences exist between the mean of radiation dose 100kV protocol and improved 80kV protocol. For this purpose test, independent samples *t*-test with unequal variance were utilised to compare the radiation doses of the 80kV protocol and standard protocol. Radiologists' findings on diagnostic confidence and image quality were also presented to confirm or reject the hypothesis.

5.3.4: Results

The study involved 100 patients who were clinically thought to have PE and were recommended to the imaging department to rule out pulmonary embolism. A total of 15 positive instances of pulmonary embolism were identified. Among this group, 10 PE diagnoses were identified within the standard CT protocol (control group), and 5 cases of PE were diagnosed in the low-dose CTPA group (test group). Alternative diagnoses, including pneumonia and emphysema, were also made in both groups; these are present in Tables 5.5 and 5.6.

A considerable decrease of approximately 66% in the effective dose was identified in terms of radiation dose while utilising an improved 80kV protocol compared to the control group. The 80kV protocol had an average effective dose that was significantly lower

(1.005mSv) compared with the standard 100kV protocol (3.03mSv), as demonstrated in figure 5.10 ($P<0.05$). This will be further discussed in the following section.

The study also found a significant improvement in control enhancement between the two groups. The average contrast enhancement in the pulmonary trunk was 643 in the low-dose protocol compared to 387 in the standard or control CTPA protocol; this is present in figure 5.11. The contrast enhancement was increased by 66% with the improved 80kV CTPA ($p<0.05$).

There was no substantial difference in signal to noise ratio, and contrast to noise ratio was found between the groups. The control group and test groups were similar in quality and suggested similar diagnostic utility. This will also be discussed later.

Table 5. 5: Alternative diagnoses with the standard CT pulmonary angiogram.

Radiologists' findings	No.
Normal studies	24
PE	10
Consolidation/infections	4
Lung cancer/metastasis	4
Atelectasis	2
Lung nodules	2
Emphysema	1
Pleural effusion	1
Lymphadenopathy	1
Pulmonary oedema	1

Table 5. 6: Alternative diagnoses with the low-dose CT pulmonary angiogram.

Radiologists' findings	No.
Normal studies	24
PE	5
Emphysema	4
Lung cancer/metastasis	4
Atelectasis	3
Lung nodules	3
Consolidation/infections	3
Pleural effusion	2
Pulmonary oedema	2

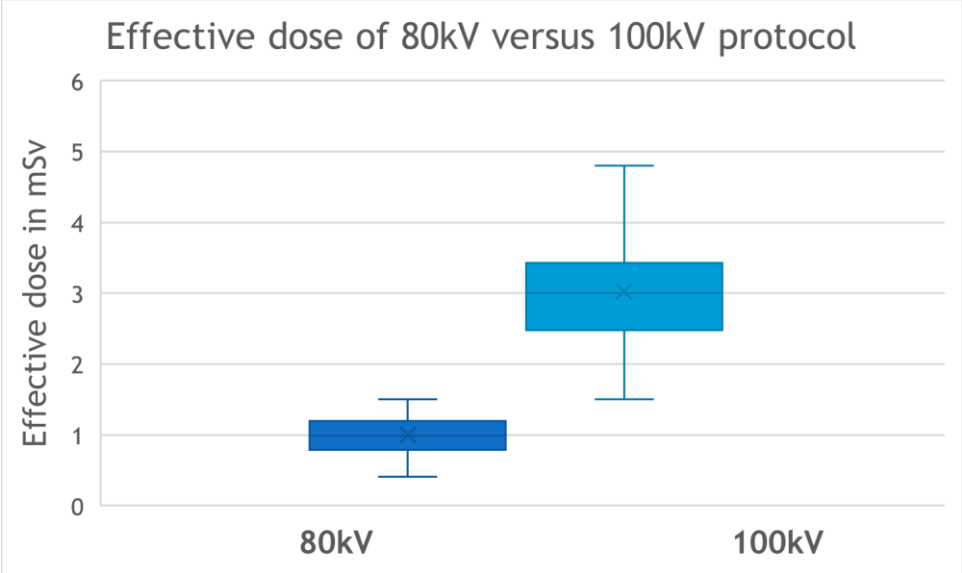


Figure 5. 10: Box-whisker plot chart distribution of radiation dose 100kV versus 80kV.

5.3.4.1: Radiation Dose Statistical Analysis

The standard CTPA 100kV protocol had a relatively higher effective dose than the 80kV protocol. The maximum and minimum exposure with the control 100kV protocol was 4.8mSv and 1.5 mSv, respectively, with a mean 3.03mSv. With the improved 80kV protocol, the maximum and minimum exposure were 1.5mSv, and 0.41mSv, respectively, with a mean 1.005mSv. The improved 80kV CTPA also had a relatively smaller variation than the 100kV protocol with respect to the interquartile range (IQR). Figure 5.10 represents the results from a descriptive data analysis of radiation dose for 100kv and 80kv protocols.

The approximately normal distribution of both data sets and appropriately sufficient sample sizes allow us to utilise the independent samples *t*-test with an unequal variance to compare the mean radiation doses of the protocols. This demonstrated that there existed a statistically significant difference ($t(60) = -17.8$, $p < 0.05$) in the radiation doses between the 80kV and 100kV protocols, table 5.7 and 5.8 illustrates these findings. The *sample sizes* of this study provide *sufficient power* (0.99) to generalise the findings.

If the null hypothesis is set as the radiation exposure at 80kV and 100kV were equal, and the alternative hypothesis was set as the radiation exposure at the improved 80kV was less than 100kV, then the alternative hypothesis can be accepted.

Table 5. 7: t-Test: two-sample assuming unequal variances.

	80KV , dose(mSv)	***100kv Dose in (mSv)***
Mean	1.01	3.03
Variance	0.066	0.57
Observations	50	50
Hypothesized Mean Difference	0	
df	60	
t Stat	-17.83	
P(T<=t) one-tail	5.76E-26	
t Critical one-tail	1.67	
P(T<=t) two-tail	1.15E-25	
t Critical two-tail	2.0	
Power (1-β)	0.99	

Table 5. 8: Statistical difference 100kV versus 80kV.

Dose	**Mean**	**SD**	**t(df)**	**p**
100kV	3.03	0.578	1.15(60)	5.77×10^{-26}
80kV	1.1	0.067		

$$H_0: \mu_{\text{Dose80kv}} = \mu_{\text{Dose100kv}}$$

$$H_A: \mu_{\text{Dose 80kv}} < \mu_{\text{Dose 100kv}}$$

***H_a*:** The alternative hypothesis validates that radiation exposure from low dose CT pulmonary angiogram is less than the radiation dose from 100kV protocol. The low-dose considerably decreased the radiation dose.

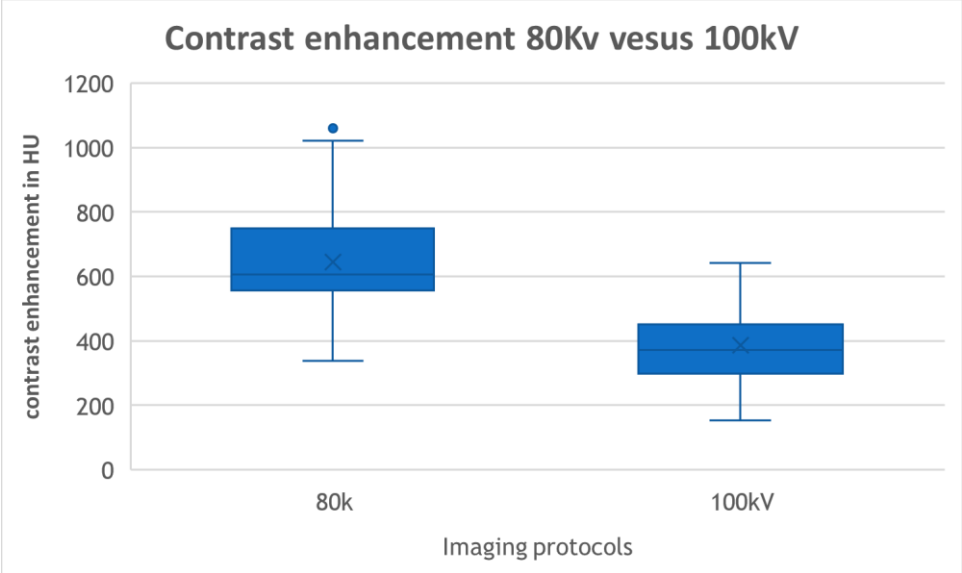


Figure 5. 11: Box-whisker plot chart displays contrast enhancement 100kV versus 80kV.

5.3.4.2: Image Quality and Contrast Enhancement Assessment

The maximum and minimum contrast enhancement with the 100kV protocol (control group) was 641 HU and 153 HU, respectively, with a mean of 387 HU. On the other hand, with the improved 80kV protocol (test group) 643, the maximum and minimum contrast enhancement was 1070 HU and 337 HU, respectively, with mean HU; this is illustrated in table 5.9. The 100kV has a relatively smaller variation than the 80kV protocol with respect to the interquartile range (IQR). If the null hypothesis is set as the contrast enhancement at 80kV and 100kV were equal, and the alternative hypothesis was set as the contrast enhancement at 80kV was more than 100kV, then the alternative hypothesis is able to be accepted.

The low dose CTPA protocol yielded acceptable image quality comparable to the standard protocol as per the radiologist assessment regarding imaging quality assessment. This is illustrated in Figures 5.12 and 5.13. With the low dose protocol, 2 cases had a suboptimal or slightly optimal imaging quality. A single patient with chronic cardiac failure demonstrated reduced opacification of contrast, and another patient had marked respiratory motion artefact. The standard 100kV protocol six examinations had suboptimal imaging quality due to respiratory motion artefact and low contrast enhancement. Therefore radiologists showed comparable confidence in detecting PE between low dose and standard CTPA protocols; this is bourne out in hypothesis testing. If the null hypothesis is set as the diagnostic confidence at improved 80kV protocol was not equal to 100k, and the alternative

hypothesis was set as the diagnostic confidence was equal, the p-value was >0.05, and the alternative hypothesis was accepted, indicating being similar between protocols. Radiologist's image evaluation, as well as Chi-square test, show that the quality of CT pulmonary angiogram in the low dose and standard 100kV protocol is similar in image quality to diagnose or exclude pulmonary embolism (Table 5.10).

The study also discovered a minor increase in image noise with the low dose protocol; this was noticeable on lung windows. The 9 cases that were identified to have minor image noise did not hamper the radiologists' diagnostic confidence in the study. Overall, the radiologists indicated no difference in diagnostic accuracy and image quality with the low-dose protocol compared to the standard protocol. The radiologist also found no difference in confidence for diagnosing alternative diagnoses such as lung atelectasis, emphysema, large nodules, masses and pneumonia.

Table 5. 9: A t-Test: two-sample assuming unequal variances.

	HU@80kv	***HU @100kv***
Mean	643.88	387.34
Variance	31691.57	12539.21
Observations	50	50
Hypothesized Mean Difference	0	
df	83	
t Stat	8.62	
P(T<=t) one-tail	1.80E-13	
t Critical one-tail	1.66	
P(T<=t) two-tail	3.67E-13	
t Critical two-tail	1.98	
Statistical sig diff (p<0.01)		
(t(83)=-8.6, p<0.01		
Power (1-β)	0.60	

$$H_0: \mu_{\text{Contrast enhancement 80kv}} = \mu_{\text{Contrast enhancement100kv}}$$

$$H_A: \mu_{\text{Contrast enhancement 80v}} > \mu_{\text{Contrast enhancement 100kv}}$$

***H_a*:** The alternative hypothesis validates that contrast enhancement from low dose CT pulmonary angiogram is greater than that from the 100kV protocol. The low dose considerably improved the contrast enhancement, and this increases diagnostic confidence and decreases suboptimal examinations.

Table 5. 10: The radiologist's overall image quality assessment in a 3-point scale rating.

Radiologist 1 Overall image quality rating	
Low dose 80kV protocol	100 kV standard imaging protocol
Excellent (score 1), *n*= 34 (68%)	Excellent (score 1), *n*= 35 (70%)
Good (score 2), *n* =14 (28%)	Good (score 2), *n* =9(18%)
Suboptimal image quality (score 3), n=2(4%) *One case has Motion artefact. * Other with reduced opacification of contrast on peripheral arteries.	Suboptimal image quality (score 3) n=6(12%), *Five cases of low contrast enhancement * One case of motion artefact.
Radiologist 2 Overall image quality rating	
Low dose 80kV protocol	100 kV standard imaging protocol
Excellent (score 1), *n*= 29(58%)	Excellent (score 1), *n*= 27(54%)
Good (score 2), *n* =19 (38%)	Good (score 2), *n* =17(34%)
Suboptimal image quality (score 3), n=2(4%) *One case has Motion artefact. * Reduced opacification of contrast on peripheral arteries.	Suboptimal image quality (score 3) n=6(12%), *Four cases of low contrast enhancement * One case of motion artefact.

$$H_0: \mu_{\text{diagnostic confidence 80kv}} \neq \mu_{\text{diagnostic confidence 100kv}}$$

$$H_A: \mu_{\text{diagnostic confidence 80kv}} = \mu_{\text{diagnostic confidence 100kv}}$$

5.3.4.2.1: Pearson's Chi-squared test

- Radiologist one: We have $\chi^2 = 3.10$, df = 2, p-value = 0.212.
- Radiologist two: We have $\chi^2 = 2.182$, df = 2, p-value = 0.335

The p-value > 0.05. So there is sufficient evidence to accept the alternative hypothesis, which indicates that diagnostic confidence and image quality of 80kV are equal to that of the 100kV standard protocol. The following images visually illustrate the image quality of the improved 80kV protocol versus the 100kV protocol.

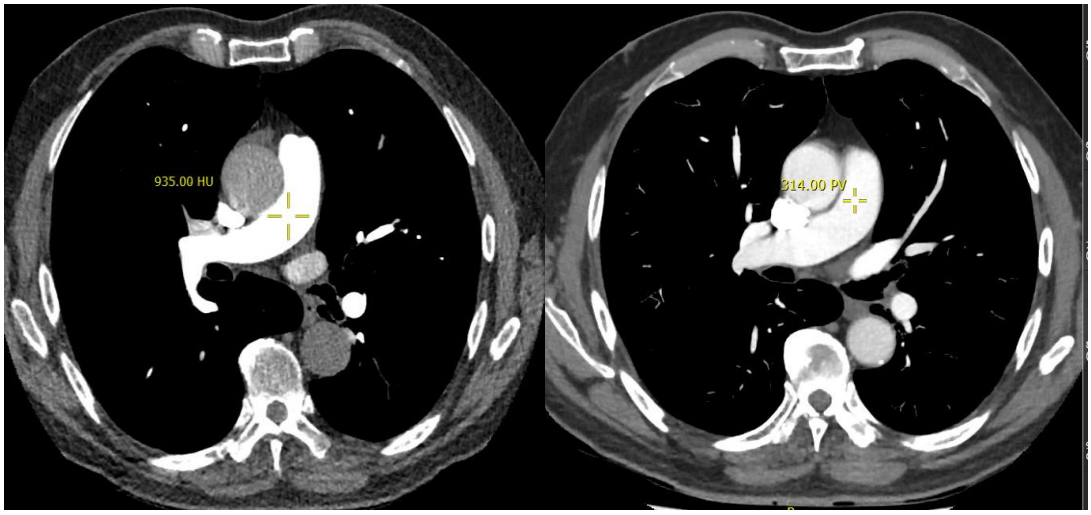


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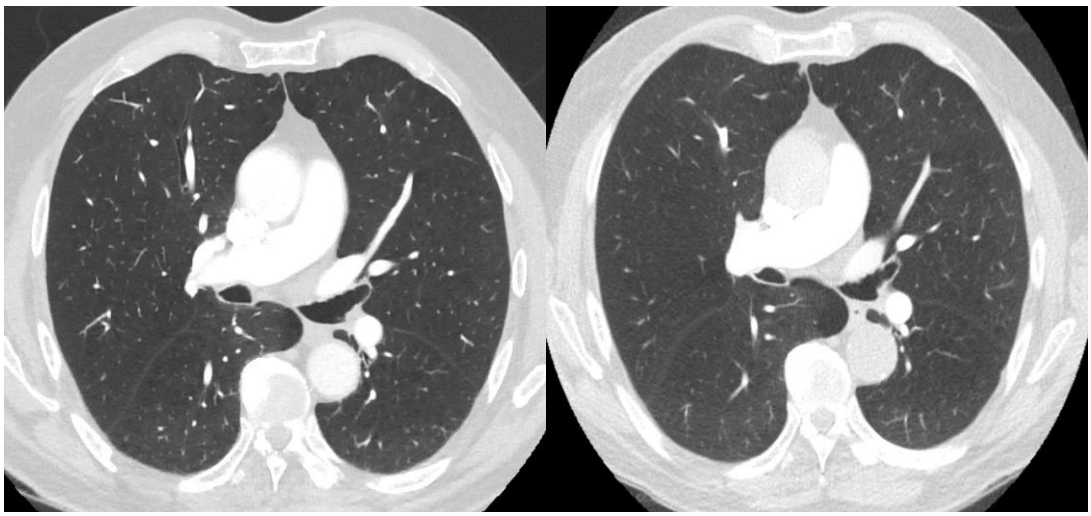
Figure 5. 12: (a) The mediastinal axial image with standard 100 kV protocol; (b) Mediastinal axial image obtained using 80kVp protocol, which is a 75% reduction in radiation dose. Images acquired ten months apart.



a b

Figure 5. 13: The lung window of the above images with no significant variance within the image quality: (a) lung window axial image obtained with the standard 100kV protocol and (b) lung window axial image obtained at the new low dose CT pulmonary angiogram protocol of 80kV.

The low dose protocol is rated to be adequate in diagnosing or excluding PE and alternative lung diseases.

5.3.5: Discussion

CTPA is an ideal assessment for PE imaging in many clinical situations. It offers accurate diagnostic specificity and sensitivity but does come at the cost of a high radiation dose. Appropriate radiation dose reduction techniques are required without damaging image

quality. With the current research, we have found that an 80 kV CTPA protocol can implement clinically with good imaging quality and low image noise.

With the new, improved 80kV protocol, image quality was maintained and rated either "excellent" or "good" in the majority of cases; in this study, 2 patients out of 50 had suboptimal or mildly suboptimal CTPAs caused by reduced contrast opacification in sub-segmental arteries and motion artefact compared to 6 patients in the standard CTPA protocol group.

The low dose protocol achieved an image quality that was objectively similar to that obtained with a standard 100kV CTPA protocol. The low dose of CTPA generated a quality image consistent with the criteria set out in the European Union Quality Criteria For Computed Tomography Working Document[230]. Image quality criteria include clear visualisation of structures, sharp visualisation of pulmonary arteries, lung parenchyma and pulmonary fissures. Clear visualisation of large, medium, and small-sized bronchi, as well as visually sharp visualisation of the border between the pleura and the thoracic wall, is adequately visualised in this protcol[230]. Within the lung window, radiologists were able to assess the dominant pattern and distribution of the alternative pathologies. Regarding spatial resolution, image noise and contrast resolution, most radiologists revealed that image quality was acceptable and accurate in diagnosing or excluding PE with lower tube voltages. With the new 80kV protocol, image quality was maintained and rated either "excellent" or "good" in most cases. In this study, two patients out of 50 had suboptimal or mildly suboptimal CTPAs caused by reduced contrast opacification in sub-segmental arteries and motion artefact compared to 6 patients in the standard CTPA protocol group

The average radiation dose was significantly lower with the improved 80kV protocol than the 100kV protocol, 1.005 and 3.03mSv, respectively. This is the lowest CTPA radiation dose available in imaging departments in Canberra and, most likely, Australia. These findings are comparable to the Szucs-Farkas et al. (2008) study, which achieved a 40% radiation dose reduction. Even though the radiation dose saving of this study is considerably higher than the above study[236].

Radiation dose is the main accomplishment of this study as high radiation exposure to patients is associated with elevated lifetime cancer risks. This study has also demonstrated that one of the limitations of previous studies, increased imaging noise, can be offset but utilising a low standard deviation for the tube voltage and improved reconstruction algorithms. Although the studies found a mild increase in the image noise among larger patients on the lung window, this was also found not to impact diagnostic confidence significantly.

This study retained the quality of the image and reduced image noise through the use

of the reconstruction algorithm FC5 and tube voltage standard deviation level 8 and the image reconstruction process AID 3D strong. The protocol also incorporated tube current modulation to track the fluctuating patient anatomy.

Other approaches to reduce radiation dose exists [121, 122]. The most prominent involving reduced mAs. The disadvantages of utilising a fixed or reduced mAs are the inability to offer a precise exposure for variable patient sizes unless an exposure chart is used, which is impractical for a busy imaging department. Thus, as with this study, an alternative technique is to reduce the kV with the current modulation; overall, this decreases radiation exposure in lower attenuation parts and provides adequate image quality.

Enhanced pulmonary arterial tree enhancement is also another significant advantage of this protocol. The study found considerable improvement in the contrast enhancement within the pulmonary arterial tree, which decreased the possibility of non-diagnostic scans; several studies also reported similar findings[134, 145].

Contrast enhancement can be attributed to low tube voltage bringing the photon energy near the iodine K-edge. In turn, it increases the pulmonary arteries' contrast enhancement. Therefore detecting the PE filling defects may be easier to identify. Furthermore, this improved enhancement will allow clinicians, particularly in the emergency setting, to diagnose PE quickly, decreasing the time most patients spend in the ED. Moreover, low voltage protocol may also be advantageous, particularly to patients with a low glomerular filtration as well as those with restricted intravenous cannula access who may profit from decreased quantity of contrast agent, but this may be an avenue for future investigation.

5.3.6: Limitations

Several limitations are noted. One of the most significant limitations is that assessing radiologists may be biased as they may prefer the brighter low dose images and assess them as better.

5.3.7: Conclusion

A low-dose CTPA protocol demonstrated a significant decrease in the radiation dose and simultaneous increased pulmonary artery contrast enhancement without compromising the diagnostic confidence or image quality.

Disclosure of Conflict Of Interest

The researchers claim no conflict of interest.

5.4: Section Four: Image Quality Qualitative Testing: Survey of Medical Doctors. Stage Two Study

The first part of this section contains the emergency medicine doctor's survey on image quality assessment. Part two of this section contains the radiologist's survey on image quality assessment.

5.4.1: Part One: Survey of Medical Doctors

5.4.1.1: Aim

This survey aimed to determine the image quality and diagnostic confidence in detecting PE with the novel CTPA protocol was acceptable to clinicians compared to the standard 100kV protocol.

5.4.1.2: Method

The questionnaires' purpose was to assess the doctors' opinions on image quality, impression, and diagnostic confidence regarding 80kV CTPA with improved image noise reduction versus standard 100kV CTPA protocol.

Because of the small number of radiologists, it was decided to get a larger sample and also question the main imaging consumer, the emergency medicine doctors. The local emergency medicine doctors are sophisticated consumers of imaging; it was found in the local setting that their knowledge and use of images was advanced. Hence they were included in the qualitative testing. The validity was preserved by checking the responses of emergency medicine doctors with the view of the reporting radiologists.

This also helped determine whether the novel protocol is useful in examining PE in the emergency medicine context.

Initially, unstructured interviews were conducted with radiology consultants to identify the key issues regarding image quality with the novel CTPA protocol. Questionnaires were formulated on the basis of the issues raised in the unstructured interviews; the opinions of the interviewed radiologists were taken into account. The radiology consultants had further input into the questions once they were formulated and presented; the modification was made if required.

The final questionnaires were presented to 50 medical doctors. The questionnaire is presented in Appendix 1.

Doctors were presented with the questionnaires when they were called to witness contrast during the CT examinations; they were then asked to evaluate the CT viewing screen images.

To reduce bias, the emergency medicine physicians were not informed of the findings obtained from the preceding studies.

5.4.1.3: Findings and Discussion

The survey found that the emergency department physicians found image quality was acceptable. They indicated they were most confident in the identification of PE as well as other lung pathologies. The majority of the interviewed physicians also indicated that they found that image noise was minimal or lower than the average image noise; both indicate acceptable imaging quality for clinical purposes. The vast majority (96%) were confident of imaging findings based on the imaging quality they assessed. A breakdown of questionnaire answers for image quality, image noise and diagnostic confidence are presented in Table 5.11.

Table 5. 11: A breakdown of Medical doctors questionnaire answers for image quality, image noise and diagnostic confidence.

Low dose CTPA Image Quality Assessment	No of doctors	Percentage
How would you rate image quality of the low dose CT pulmonary angiogram?		
Excellent	28	56%
Good	22	44%
Somewhat suboptimal		
Unacceptable for diagnostic purposes		
How would you rate the image noise of the low dose CT pulmonary angiogram?		
Minimal image noise	28	56%
Less than average noise	13	26%
Average noise	9	18%
Unacceptable image noise		
How confident are you in the detection of PE in this low dose CT pulmonary angiogram?		
Completely confident	48	96%
Probably confident	2	4%
Somewhat suboptimal		
Unacceptable for diagnostic purposes		
What is your preferred Imaging Modality?		
Low dose pulmonary angiogram	50	100%
V/Q scan	0	

As illustrated in above table 5.11, the image noise was satisfactory and the emergency department physicians found adequate imaging quality for clinical purposes.

5.4.1.4: Conclusion

The main imaging consumer, the emergency medicine doctors, indicated the low dose CTPA protocol had acceptable image quality, image noise, and diagnostic confidence. The novel

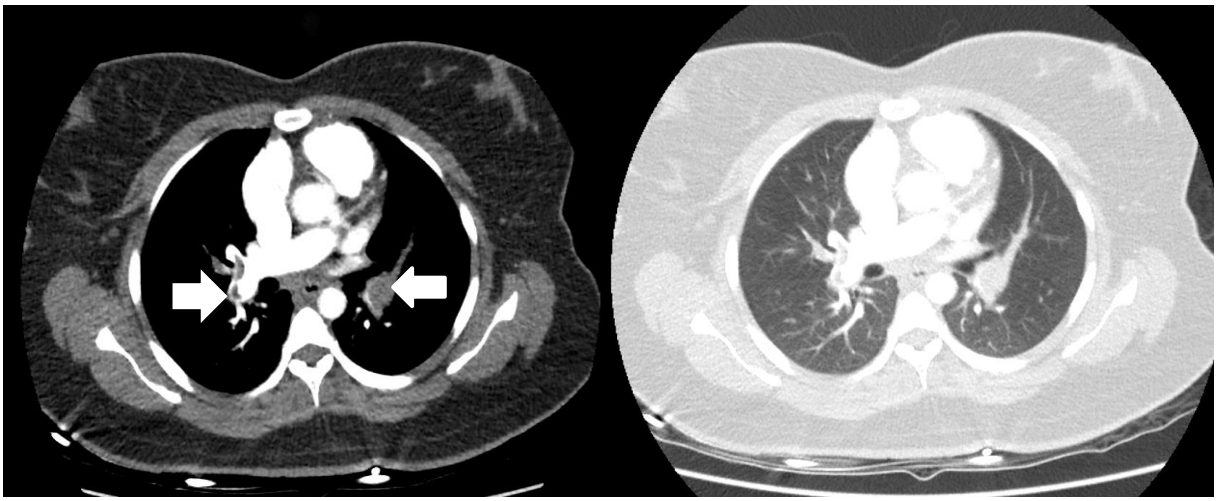
protocol was found to have either excellent or good imaging quality. Image noise was in the majority of cases rated as acceptable as or lower than the average. The majority of respondents were entirely confident in the diagnosis quality of the imaging.

5.4.2: Part Two: Radiologist Follow up Interview

A further test of image quality is whether it serves the purpose for which it was acquired, namely to diagnose or exclude PE. To ascertain radiologists' opinion regarding image quality, image noise, and diagnostic confidence, follow up unstructured interviews were conducted with two reporting radiologists. Reporting radiologists graded the quality of the imaging initially by reviewing the images for image noise, the artefact (motion artefact, respiratory artefact), the image quality of soft tissue and bony structures and diagnostic confidence. The same criteria were utilised amongst all the radiologists. A standardised image set was utilised, adequate viewing conditions and equal durations for interpretations were provided to ensure unbiased and comparable results.

5.4.2.1: Findings and Discussion

The two reporting radiologists expressed their views on image quality and diagnostic confidence and whether imaging quality at 80kV image quality was equal to the 100kV protocol. Radiologists were confident in diagnosing PE and alternative focal lung ailments on the novel CTPA protocol. The figure below illustrates the image quality of the improved 80kV protocol.



a b

Figure 5. 14: A 23 years old patient with extensive pulmonary emboli(a). (b) Illustrates FC51 with lower image noise. Contrast enhancement and image quality are rated to be of high quality. The effective dose radiation dose was 0.78 mSv.

They indicated that the image quality and image noise was equal to that obtained at 100kV (among patients with less than 105kg). The answers of the radiologists are presented in Table 5.12

Table 5. 12: Radiologit's questionnaire answers for image quality on 100kV versus 80kV.

Questions	Radiologist 1	Radiologist 2
Q1. How would you rate the image noise of the low dose CT pulmonary angiogram?		
1 = Minimal image noise		
2 = Less than average noise	Images have less than average noise	The images have less than average noise
3 = Average noise,		
4 = Unacceptable image noise.		
Q2. How would you rate the image quality of the low dose CT pulmonary angiogram?		
1 = Unacceptable for diagnostic purposes,		
2 = Somewhat suboptimal,		
3 = Good,	Good image quality	
4 = Excellent		Excellent image quality
Q3. How confident are you in the detection of PE in this low dose CT pulmonary angiogram?		
1 = Poor confidence,		
2 = Confident only for limited clinical situation,		
3 = Probably confident,		
4 = Completely confident	Completely confident	Completely confident
Q4. This protocol should be used as a gold standard for the diagnosis of pulmonary embolism		
Strongly agree		Strongly agree
Agree	Agree	
Neither agree nor disagree		
Disagree		
Strongly disagree		
Q5. The confidence in detecting PE at 80kV is the same image quality to that set at 100kV?		
Strongly agree		
Agree	Agree	Agree
Neither agree nor disagree		
Disagree		
Strongly disagree		

As illustrated in Table 5.12, the radiologists were confident about the novel CTPA protocol's strength in detecting PE. Image quality is illustrated in figure 5.14.

As the reporting radiologists were confident about the novel CTPA protocol's findings, the imaging department continued to utilise it for routine work.

Also, with ongoing assessment over the last 14 months, no significant image quality or image noise issue has arisen with the novel low dose CTPA protocol.

5.4.2.2: Radiologists' opinion on the limitation of low dose

The low dose is not standard imaging for all lung diseases; the radiologists stated they prefer the standard CT chest for interstitial lung diseases. Although image quality is lower than the standard CT chest, however, with further improvement in this protocol (mainly SD tube current), radiologists were able to evaluate some chronic lung diseases with low dose CTPA satisfactorily. The image showing interstitial lung disease is demonstrated in figure 5.15. The image shows an interstitial pattern with a honeycomb which is pulmonary fibrosis.

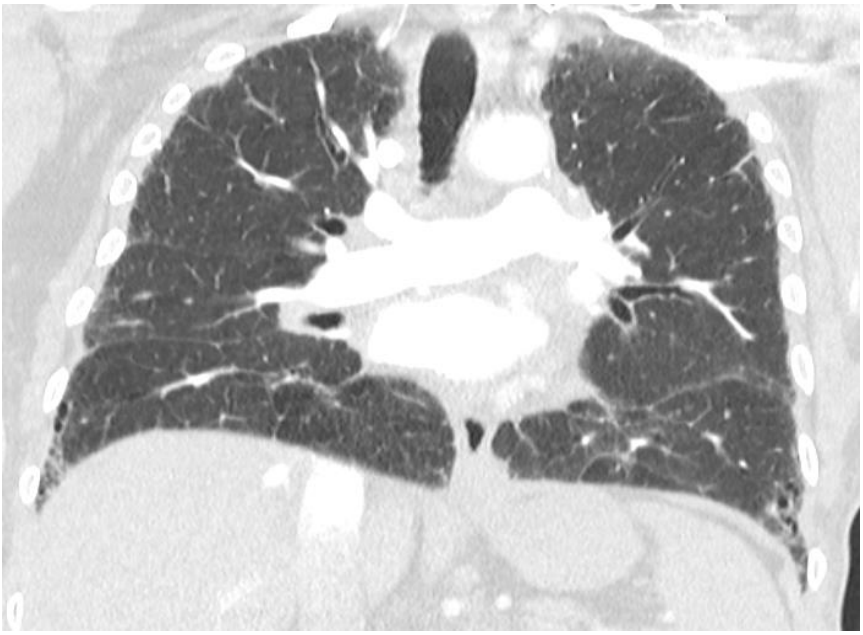


Figure 5. 15: Bilateral peripheral interstitial pattern with honeycombing and traction bronchiectasis keeping with pulmonary fibrosis.

Figure 5.16 shows a pulmonary angiogram showing good contrast enhancement of the same patient; no PE detected in this case; symptoms are likely due to chronic lung disease.

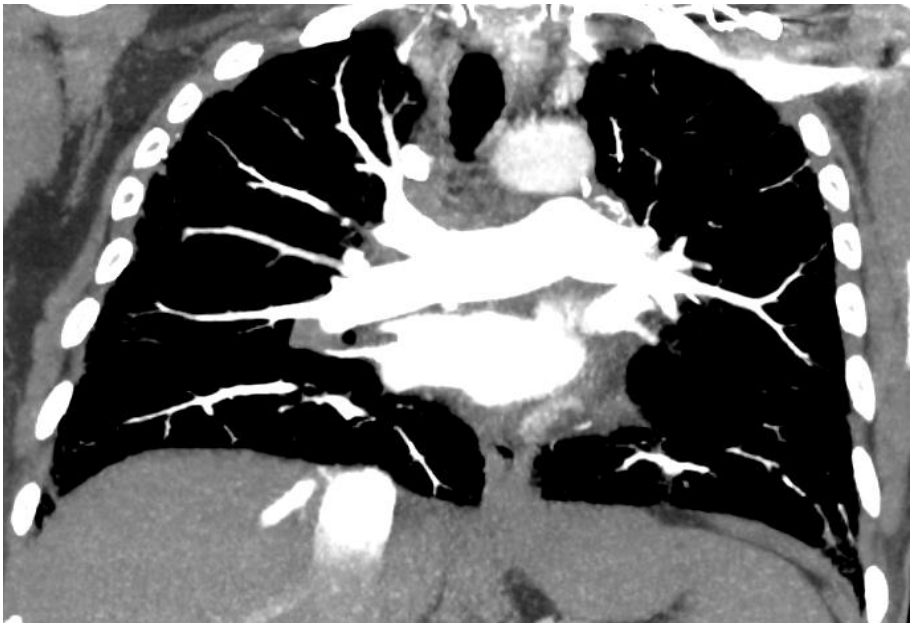


Figure 5. 16: Mediastinal windows of the above patient showing good contrast enhancement.

With the improvement in this low dose protocol, it is possible to evaluate chronic lung diseases. The interstitial pattern with a honeycomb of pulmonary fibrosis is visible, as shown in the above images.

Chapter summary, the current research found that an 80 kV CTPA protocol can implement clinically with good imaging quality and low image noise. This improved 80kV decreased radiation dose and simultaneous increased pulmonary artery contrast enhancement without compromising the diagnostic confidence.

Chapter 6: Strategies to Reduce Suboptimal CT Pulmonary Angiograms

Chapter six contains five sections. Section one discusses approaches to reduce the rate of suboptimal CT Pulmonary Angiograms. Section two discusses imaging pregnant patients with suspected PE with reduced radiation dose and suboptimal scans without compromising image quality. Section three discusses the validation of the protocol validity and reliability. Section four discusses strategies to decrease failure rate and radiation dose on larger patients. Section five discusses volume scanning, which is a new method of scanning pulmonary embolism

6.1: Section one: Prospective Comparison Study Two:

Approaches to Reduce the Rate of Suboptimal CT Pulmonary Angiograms

6.1.1: Abstract

The purpose of this study was to reduce the occurrence of suboptimal image quality while improving contrast enhancement among patients investigated with CT Pulmonary Angiography (CTPA) for suspected Pulmonary Emboli (PE) by utilising an increased injection rate, lowering tube voltage (80kV) and gentle breath-holding with an open mouth.

Method

One hundred forty patients with clinical features of acute PE were included and were divided into two groups. In group A, patients were imaged with the standard 100kV CT pulmonary angiogram protocol with standard deep inhalation and an immediate breath-hold prior to scanning. In group B, patients were asked to gentle breath-hold with an open mouth and were scanned with the 80kV protocol. Patients underwent imaging with a 320-row multi-detector Toshiba Aquilion One Genesis Edition in the absence of the proprietary radiation reduction software known as forward projected model-based Iterative Reconstruction Solution (commercial acronym ‘FIRST’).

Results

The study found a reduced rate of suboptimal examinations and a significant increase in contrast enhancement of the pulmonary arterial tree with gentle breath-hold open mouth technique 80kV scanning protocol (Group B). The mean Hounsfield unit was 599 HU in Group B compared to 351 HU in Group A. A considerable decrease in the effective dose was observed with an average effective dose of 1.1mSv in Group B versus 3mSv in Group A.

Conclusion

A gentle breath-hold with an open mouth as well as a low tube voltage of 80kV allows for considerably increased enhancement of the pulmonary arterial tree on CTPA with a lower rate of suboptimal examinations and a significant reduction in patient radiation dose without affecting the image quality.

6.1.2: Introduction

Pulmonary Embolism (PE) is defined as a condition in which one or more pulmonary arteries within the lung become blocked by blood clot thrombi originating from the distant sites. PE represents a significant threat to the ageing population[237]. The reported incidence is approximately 3 per 1000 patients annually[96]. In most cases, it is due to a thrombus forming within the pelvic or lower limb veins breaking off and travelling to the lungs. Embolised fragments of the tumour, air locules, injected recreational drugs, and fat lobules (resulting from long bone fracture) may also lodge in the pulmonary arterial tree and present in a similar manner[238].

Typical symptoms include dyspnoea and chest pain. However, these are not specific to PE and may be seen in many conditions such as infection, inflammation (including hypersensitivity) and fluid overload, to name a few. This makes diagnosing PE a challenge, particularly in patients with comorbidities. As patients can deteriorate without early treatment, hence rapid diagnosis is essential for prompt management.

CT Pulmonary Angiogram (CTPA) is the current gold standard for aiding diagnosis of PE and alternative diagnoses that cause the presenting symptoms[105]. However, the success of CTPA has led to overuse, with only 11% of the performed scans found to be positive in this imaging department.

CTPA examinations are not always of diagnostic quality; many suboptimal examinations are often made up of non-diagnostic and low-contrast enhanced studies. These scans contribute to unnecessary radiation dose[28].

Several factors contribute to suboptimal scans, including poor venous access, low contrast enhancement in segmental/subsegmental pulmonary arteries, an incorrectly placed region of interest (ROI), Valsalva manoeuvre, inappropriate breathing (patient factors/technologist instructions), insufficient cannulation-flow rate and respiratory motion artefact. Additionally, tachycardia leads to an increased heart rate, resulting in an irregular ventricle ejection associated with low contrast volume and pulmonary trunk enhancement. In this situation, the pulmonary trunk shows high contrast enhancement at the monitored slice, but once the scan reaches the pulmonary trunk, peak contrast enhancement HU has often passed into the suboptimal range.

Similarly, suboptimal examinations are frequent amongst patients with high body mass index (BMI) utilising a 120kV scanning protocol. A quality assurance assessment within this department has demonstrated that the number of suboptimal scans with poor contrast enhancement increased substantially among patients weighing greater than 100kg, with 24% of the patients surveyed in this group having suboptimal or low contrast-enhanced scans with the 120kV protocol.

Another significant additional factor contributing to suboptimal CTPA examinations was low contrast enhancement due to the unintentional Valsalva manoeuvre during breathing. Valsalva manoeuvre is exaggerated by deep inspiration breath-hold against a closed glottis resulting in a varied flow of blood from the abdomen vessels back to the heart, potentially diluting the contrast media returning to the heart and hence to the pulmonary trunk, hence leading to suboptimal images

This research proposed a study to examine alternative ways to reduce respiratory motion artefacts and Valsalva and increase contrast enhancement in CTPA without reducing image quality.

The primary aim was to decrease the number of suboptimal images amongst patients with suspected PE by increasing contrast enhancement of the pulmonary arteries by utilising a gentle breath-hold with an open mouth technique and a high injection rate and lower tube voltage.

6.1.3: Method

Ethics approval was granted from the Australian National University and the Australian Capital Territory Public Hospital Ethics Committee Review Committee. One hundred forty patients eligible patients were enrolled before undergoing CTPA and split into two separate groups of 70 (Group A and Group B).

Group A patients were allocated to a routine standard of 100kV CT pulmonary angiogram protocol and were required to take a deep breath in and hold it immediately prior to scanning as per standard practice. A reconstruction algorithm-kernel FC53 with tube current modulation was used in combination with an image reconstruction protocol 'AID 3D' standard and an effective mAs of 215, also as per standard practice. The scanner automatically instructed them to perform the breathing instruction. The data was recorded prior to the implementation of the low dose CTPA protocol for group B.

Group B patients were allocated to the low-dose CTPA protocol with the image reconstruction process 'AID 3D Strong' and a standard deviation of the tube current level 8 (Tradename: 'Sure Exposure 3D'). An effective mAs of 258 and tube voltage of 80kV with tube current modulation were utilised. A reconstruction algorithm utilising a kernel FC51 was utilised to provide reduced noise. A superior injector apparatus was used to decrease the failure rate of the cannula. Finally, patient education on breathing with active coaching and relaxation techniques was provided to achieve a gentle breath-hold with an open mouth to decrease Valsalva and motion artefact.

Peer-matching was utilised to form a cohort of comparable patients. In peer matching, both control and test groups consisted of 35 female and 35 male patients. The two groups were to have comparable age and weight distributions. The mean age of the participants in control group A was 60.0±19.98 years versus 57.5 ±20.67 for Group B. The mean weight of the participants in group A was 68.94±12.55 years versus 68.54 ±13.22 for Group B.

All patients were scanned on a 320-row multi-detector Toshiba Aquilion One Genesis Edition, without 'FIRST', a propriety software used for radiation reduction. They were also given 40-70mL iodinated contrast medium iopromide 370 mg/mL (Bayer, tradename Ultravist) with 50mL saline flush as per standard protocol with contrast medium dosing based on weight. The scan was performed using an 18-G cannula inserted in the cubital fossa. A minimum flow rate of 4.5 mL/sec flow rate was used with an unmodified dual-head injector. Ulrich' brand of an

injector was utilised with 18 ml saline testing and the capability to change both flow and pressure during contrast administration. Automatic bolus tracking was utilised with scanning triggering with 180 HU in the pulmonary trunk, as is common practice.

A region of interest was positioned at the pulmonary trunk to evaluate contrast enhancement, specifically to achieve the correct measurement in Hounsfield units (HU). The minimum ROI size was 5 mm^2. Images that demonstrated a contrast enhancement with more than 210 HU in the main pulmonary artery were defined as having satisfactory contrast enhancement to detect PE. The images were considered suboptimal or non-diagnostic when contrast enhancement was less than 210 HU and/or when the two reporting radiologists graded the images as non-diagnostic or suboptimal.

In this study, exclusion criteria were: patients under the age of 18 years, patients with renal impairment defined as estimated glomerular filtration rate (eGFR) < 30 $ml/min/1.73m^2$, chest depth of greater than 30 cm, or weigh over 105 kg. The last two exclusion criteria were set as they are parameters for using higher tube voltage.

The data were presented in terms of statistical properties such as minimum, mean and maximum (with confidence interval) of radiation doses and contrast enhancement. The study also presented the frequency distribution of the list of PE differential diagnoses. A side-by-side box plot is presented to visualise the differences and distribution of the radiation dose and contrast enhancement. The image quality of both groups was evaluated using a 3-point scale. For example, score 1: Images with no diagnostic issue and/or minimal noise (excellent image quality). Score 2: Images with no diagnostic problem but with minor increased image noise (good image quality). Score 3: Images with noticeable image quality issues and/or significant image noise (suboptimal image quality). In the case of discordance in scores in the study group's subjective image analysis, images were re-analysed, and a consensus was reached.

A hypothesis test was conducted to test if significant differences exist between the mean of radiation dose 100kV protocol and improved 80kV protocol. For this purpose, a test independent sample t-test with unequal variance was utilised to compare contrast enhancement and the 80 kV protocol's radiation doses versus the 100kV standard protocol. The alternative hypothesis using the test for equality of proportions with continuity correction is utilised to validate if the rate of suboptimal examinations from the low dose CT pulmonary angiogram is significantly lower than that from the 100kV protocol.

6.1.4: Results

The study involved 140 patients that were suspected clinically of having a pulmonary embolic disease and were recommended to the imaging department to rule out pulmonary embolism.

Sixty-three patients in Group A (90%) had negative CTPA examinations, while only seven patients had positive PE results. Additional diagnoses in Group A comprised of pneumonia, emphysema, atelectasis, incidental pulmonary nodules, inflammation changes, fibrosis, bronchitis, lung metastasis, and pleural effusion.

Sixty-six patients in Group B (94.3%) had a negative CTPA scan, and only four positive (5.7%). The most prevalent alternate diagnoses were emphysema, pneumonia, and atelectasis.

There were three records with motion artefacts in group A, and suboptimal contrast attenuation was identified among seven patients. In group B, one CTPA had reduced the contrast enhancement of the subsegmental pulmonary arteries, and a second other examination had a respiratory movement artefact. The total suboptimal studies amounted to 10 cases in group A, while only 2 cases were recorded in group B. In the suboptimal studies, images were thought to be suboptimal due to low contrast enhancement or motion artefact, radiologists were able to exclude large pulmonary emboli with the exception of one case with markedly suboptimal (150 HU) contrast enhancement in the standard protocol group A.

The contrast enhancement increased noticeably with the low dose protocol/group B with an average Hounsfield unit (HU) of 599 HU compared to 351 HU in group A, as illustrated in figure 6.1.

Most importantly, a substantial drop in the radiation dose was observed in group B, with the average adequate dose noticeably lower at 1.1mSv, with group A achieving 3mSv (figure 6.2)

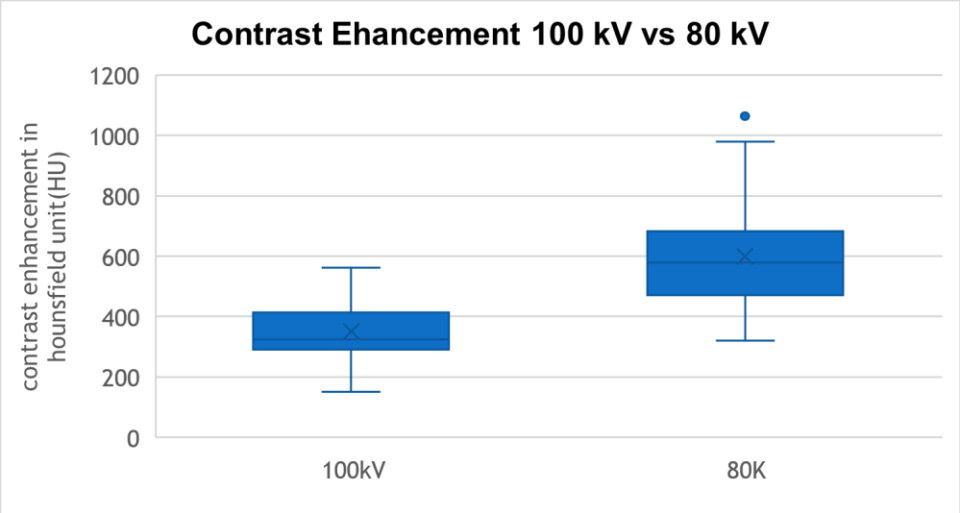


Figure 6. 1: Box-whisker plot chart displays a significant contrast enhancement in the tube with low voltage protocol.

6.1.4.1: Image Quality and Contrast Enhancement Assessment

The above box-whisker plot shows a distribution that indicates a significant contrast enhancement improvement with the low dose protocol. The maximum and minimum contrast enhancement of the 100 kV was 563 HU and 150 HU, respectively, with a mean of 351 HU. On the other hand, the maximum and minimum exposure the 80 kV was 1064 HU and 320 HU, respectively, with a mean of 599 HU. The 100 kV has a relatively smaller variation than the 80 kV protocol with respect to the interquartile range (IQR).

Figure 6.3 and figure 6.4 visually demonstrate image quality at 80kV versus 100kv, respectively.

6.1.4.2: Statistical Analysis

The contrast enhancement of the two protocols follows a normal distribution with reasonably varying variances. Hence, the appropriate statistical test for comparing the mean of the groups is an independent sample *t*-test with unequal variance.

The statistical analysis measured contrast improvement between the 100 kV and the 80 kV protocols. Significant differences ($t(75) = 9.1$, $p < 0.05$) were identified between the 100 kV and the 80kV exposures. The contrast enhancement of the 80 kV at 599 HU was found to be greater than that of the 100 kV at 351 HU; this is visually demonstrated in Table 6.1.

If the null hypothesis is set as the contrast enhancement at 80 kV and 100 kV were equal, and the alternative hypothesis was set as the contrast enhancement at 80 kV is greater than 100 kV, then the alternative hypothesis is able to be accepted.

Table 6. 1: Contrast enhancement t-Test unequal variances.

Protocols	***80Kv HU***	***100kV HU***
Mean	598.47	351.1
Variance	27186.42	9297.45
Observations	70	70
Hypothesized Mean Difference	0	
df	111	
t Stat	10.83	
P(T<=t) one-tail	2.11E-19	
t Critical one-tail	1.65	
P(T<=t) two-tail	4.22E-19	
t Critical two-tail	1.98	
Power (1-β)	0.79	

***H_a*:** The alternative hypothesis endorses that contrast enhancement from low dose CT pulmonary angiogram is greater than that from 100kV protocol

$$H_0: \mu_{\text{Contrast enhancement 80kv}} = \mu_{\text{Contrast enhancement 100kv}}$$

$$H_A: \mu_{\text{Contrast enhancement 80kv}} > \mu_{\text{Contrast enhancement100kv}}$$

6.1.4.3: 2-sample test for equality of proportions

If the null hypothesis is set as the rate of suboptimal examinations at 80 kV protocol is equal to 100 kV protocol, and the alternative hypothesis was set as the suboptimal examinations at 80 kV is less than 100 kV protocol, then the alternative hypothesis is able to be accepted when there are less suboptimal studies. Table 6.2 shows a 2-sample test for equality of proportion.

Table 6. 2: Sample test for equality of proportions.

```
test <- prop. Test(x = c(2, 10), n = c(70, 70), correct=TRUE,
alternative='less')
test
2-sample test for equality of proportions with continuity
correction
data:  c(2, 10) out of c(70, 70)
X-squared = 4.4661, df = 1, p-value = 0.017
alternative hypothesis: less
sample estimates:
   prop 1         prop 2
0.02857143     0.14285714
```

$$H_0: \mu_{\text{suboptimal exams 80kv}} = \mu_{\text{suboptimal exams 100kv}}$$

$$H_A: \mu_{\text{suboptimal exams 80kv}} < \mu_{\text{suboptimal exams 100kv}}$$

The statistical analysis measured the rate of suboptimal examination between the 100 kV and the 80 kV protocols. Significant differences (t (75) =9.1, p= 0.017) were identified between the 100 kV and the 80kV exposures at 0.05% level.

***H_a*:** The alternative hypothesis is validated using the test for equality of proportions with continuity correction; the rate of suboptimal examinations from the low dose CTPA is significantly lower than that from the 100 kV protocol. Hence this study achieved the aim of decreasing the rate of suboptimal image quality among patients undergoing CTPA

6.1.4.4: Radiation Dose

The standard CTPA 100 kV had a relatively higher effective dose; the maximum and minimum exposure for the 100 kV was 4.7 mSv and 1.3 mSv, respectively, with the mean of 3 mSv. On the other hand, the maximum and minimum exposure in the 80 kV group was 1.6 mSv and 0.4mSv, respectively, with a mean of 1.1 mSv.

The lower dose of 80 kV results in a smaller variation than the 100 kV protocol, as seen with respect to the interquartile range (IQR); this is visually demonstrated in Figure 6.2.

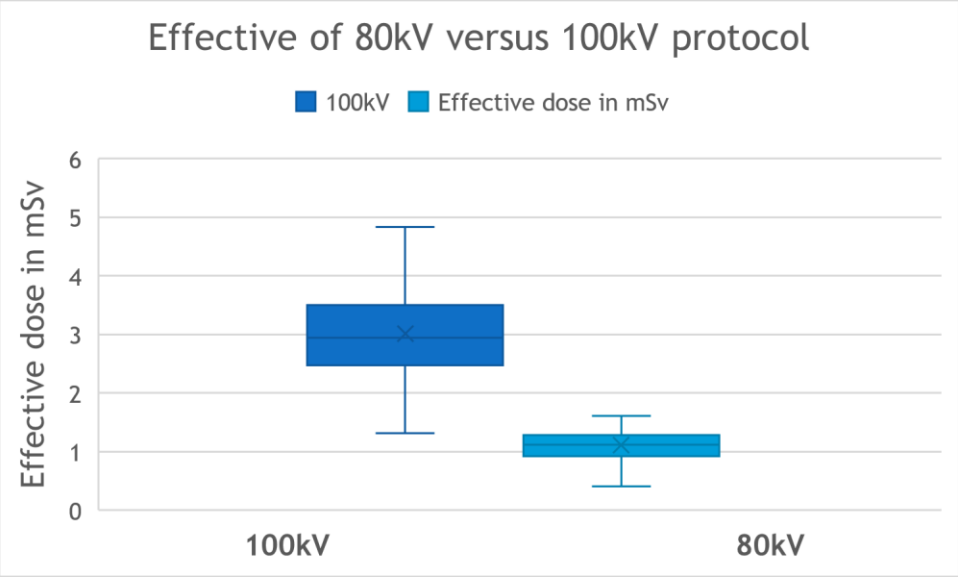


Figure 6. 2: Box-whisker plot chart displays distribution radiation dose 100kV versus 80kV.

The chart represents the results from a descriptive data analysis of radiation dose for 100 kV and 80 kV protocols.

The approximately normal distribution of both datasets, along with reasonably large sample sizes, allowed the use of independent samples *t*-test with an unequal variance to compare the mean radiation doses of the protocols (Table 6.3 and 6.4). Using this test there is a statistically significant difference ($t(84) = -19.4$, $p < 0.05$) in the radiation doses between 80-kV and 100 kV protocols. Specifically, it was found that the mean radiation dose was significantly lower for the 80 kV protocol (1.1 mSv) than for the 100 kV one (3 mSv). The sample size of this study provides sufficient power (0.99) to generalise the findings.

Suppose the null hypothesis is set as the radiation exposure at 80 kV and 100 kV was equal. The alternative hypothesis was set as the radiation exposure at 80 kV is less than 100 kV. In that case, the alternative hypothesis can be accepted.

Table 6. 3: Radiation dose t-test.

	80Kv Dose	***100kV dose***
Mean	1.10	3.01
Variance	0.068	0.60
Observations	70	70
Hypothesized Mean Difference	0	
df	84	
t Stat	-19.40	
P(T<=t) one-tail	4.31E-33	
t Critical one-tail	1.66	
P(T<=t) two-tail	8.62E-33	
t Critical two-tail	1.98	
Power (1-β)	0.99	

Table 6. 4: Radiation dose t-test variance.

Dose	**Mean**	**Variance**	**t(df)**	**p**
100kV	3.014	0.60	8.6(84)	4.315X 10^{-33}
80kV	1.1	0.068		

***H_a*:** The alternative hypothesis validates that radiation exposure from low dose CT pulmonary angiogram is less than the radiation dose from 100kV protocol

$$\mathrm{H}_0\colon \mu_{\mathrm{Dose\ 80kv}} = \mu_{\mathrm{Dose100kv}}$$

$$\mathrm{H}_\mathrm{A}\colon \mu_{\mathrm{Dose\ 80kv}} < \mu_{\mathrm{Dose100kv}}$$

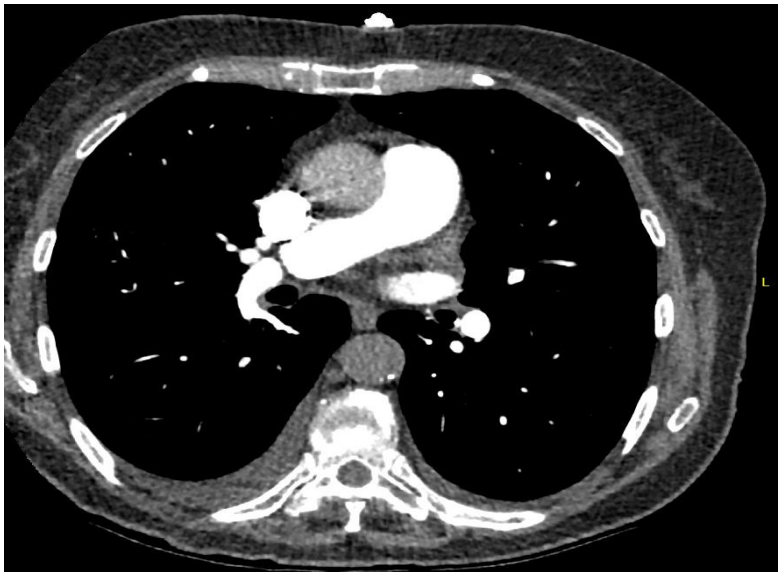


Figure 6. 3: The 80kV with a high contrast enhancement at 986 HU, with a low effective dose amounting to 0.9mSV.There is pleural effusion and process of inflammation that would likely be diagnosed as an infection.

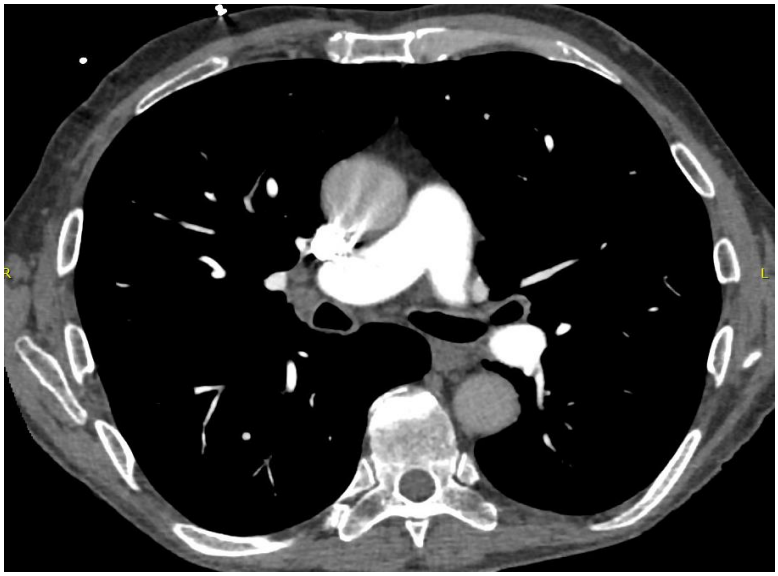


Figure 6. 4: Represents the 100kV protocol with outstanding contrast enhancement at 401HU and an effective dose-measuring 2.9mSv. The report revealed severe lung emphysema and a 2cm nodule observed in the right lower lobe.

6.1.5: Discussion

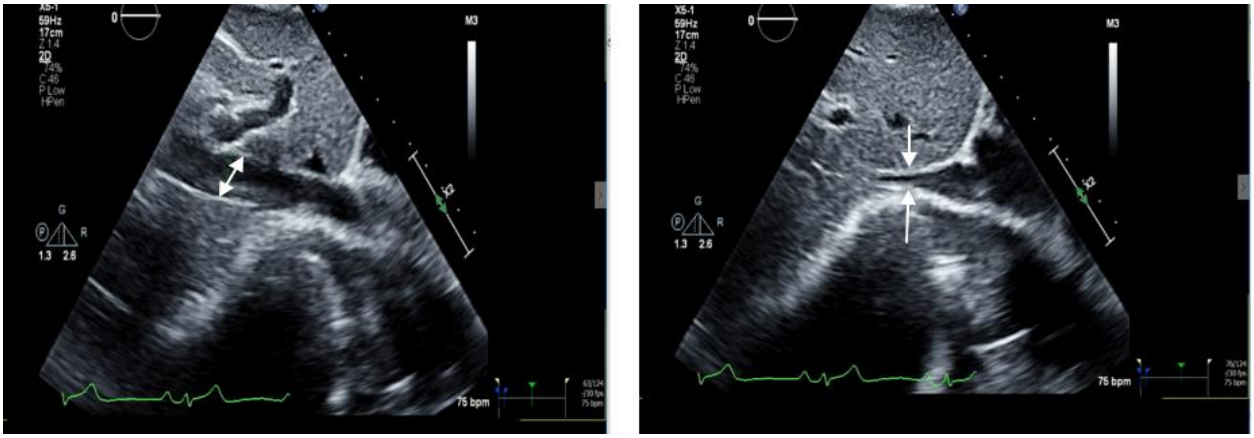
The study explored ways to reduce the occurrence of suboptimal image quality and demonstrated the benefits of a gentle breath-hold with the mouth being opened using an improved 80kV protocol.

The propensity to Valsalva with deep inspiration and a higher tube voltage on standard protocols is thought to be the leading cause of lower contrast enhancement of the pulmonary arterial tree. The mechanism of how the Valsalva manoeuvre results in a lower contrast enhancement may be due to its effects on blood flow dynamics and venous return to the heart, causing irregular contrast enhancement.

As an aside, echocardiography assessment performed during this research project in the cardiac department revealed a deep inspiration breath-hold immediately prior to scanning causes obstruction of the inferior vena cava and superior vena cava (Figure 6.5). This led to a drop in cardiac filling and a fall in cardiac output. At the end of Valsalva, venous return to the right atrium increased significantly. The increased blood flow may cause unenhanced blood from the abdomen to dilute the pulmonary tree's enhanced blood when the right atrium blood flow increases at the end of the Valsalva. Consequently, breathing dynamics disrupt contrast flow to the heart to a varying and therefore impact contrast enhancement of the pulmonary arteries in an unpredictable manner[239].

Kuzo et al. used magnetic resonance imaging to evaluate blood flow in the superior and inferior vena cava in different phases of respiration. The researchers established that deep inspiration in the CTPA study increased the amount of blood returning from the inferior vena cava and caused dilution of contrast that reaches the pulmonary trunk[240]. Other studies also agreed with these findings [172, 241, 242]. It is not entirely clear the mechanism by which the increased intrathoracic pressure during the Valsalva affects the inflow of injected contrast agents, though superior vena cava collapse has been proposed.

Therefore avoiding deep inspiration immediately prior to the pulmonary CTA data acquisition appears to reduce this unwanted effect in this setting. A gentle breath-holding during data acquisition has been demonstrated to decrease CTPA suboptimal studies effectively.



a b

Figure 6. 5: Echocardiography displays a significant reduction in vessel lumen diameter on inspiration with Valsalva manoeuvre, a) expiration b) inspiration. Inferior vena cava diameter reduced from 1.5cm to 0.6cm.

Figure 6.6 demonstrates the right ventricle with a volume of 18cm2; this is less than obtained when directed the patient to perform a deep breath-hold.

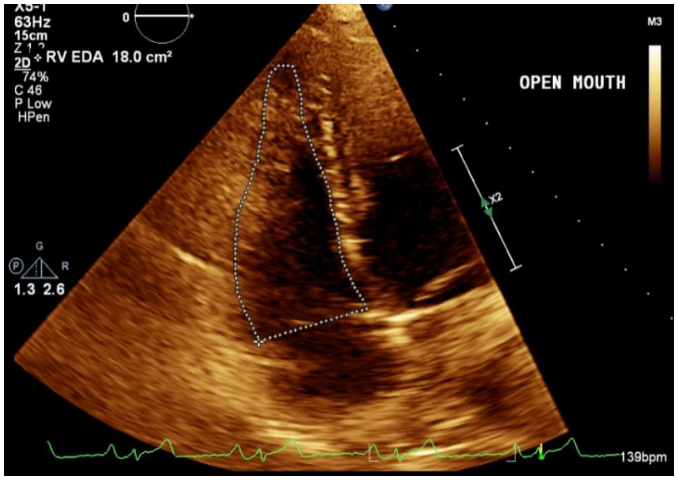


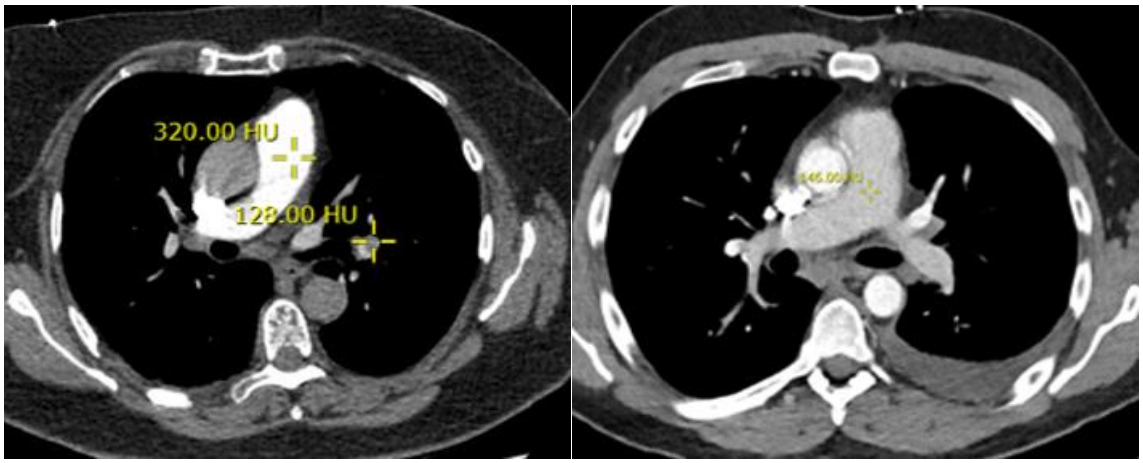
Figure 6. 6: Echocardiography with a gently breath-hold with an open mouth. In this technique, the right ventricle displays the volume of 18cm2 and has been proven to reduce the risk of Valsalva manoeuvre.

The results of this study would indicate the imaging departments may not be required to direct patients to perform deep breath-hold with CTPA studies. Instead, a viable alternative is to direct patients to gently hold their breathing with their mouth open, as per the improved 80kV protocol. In this single-centre study, this approach has been shown to produce diagnostic studies and reduce the rate of Valsalva and suboptimal studies.

The improved 80kV protocol improved contrast enhancement in the pulmonary arteries and reduced the occurrence of non-diagnostic scans. Using this protocol, no low-contrast enhancement cases occurred in this study, the lowest recorded Hounsfield unit being 320 HU, as seen in figure 6. 7 (image a). The attenuation coefficient of iodine increases significantly as photon energy decreases toward the K-edge energy of 33 keV[151].

The resulting CTPA examinations demonstrated good pulmonary arterial enhancement with good diagnostic confidence. Pulmonary emboli, however, appeared more conspicuous, which allowed greater diagnostic confidence.

Figure 6.7's image (a) was performed with a gentle breath-hold with an open mouth with 80kV, and image (b) was on deep inspiration breath-hold with 100kV.



a b

Figure 6. 7: image (a) became better at detecting emboli at (128 HU), even at the lowest enhancement of 320 HU in 80 kV protocol. Image (b) 100kV protocol with contrast enhancement being at 146HU, denying the chance to diagnose the condition accurately.

Image (a) is the lowest recorded Hounsfield unit being 320 HU; lower tube voltage allows greater diagnostic confidence in this case. With the 100kV protocol, it is likely impossible to clearly visualise feeling defect, which is 128 HU in the image (b).

More discussion of results, implication, what it means to the medical imaging department in the discussion/conclusion chapter.

6.1.6: Limitations

An essential limitation of this study was that results were from a single centre utilising a single scanner. Larger sample size with multiple centres would be valuable in confirming this study's results.

6.1.7: Conclusion

CTPA scanning with a gentle breath-hold with an open mouth in an 80kV protocol permits CTPA to be acquired with a considerable reduction in patient radiation dose, less suboptimal examinations, and higher contrast enhancement relative to current scanning protocols without compromising image quality.

6.2: Section Two: Optimised CT Pulmonary Angiogram Protocol in Pregnant Patients with Suspected Pulmonary Embolism.

6.2.1: Aim

The main purpose of this article is to highlight methods to decrease both radiation dose and non-diagnostic studies in pregnant patients without affecting image quality.

6.2.2: Introduction

Pregnancy and postpartum are associated with increased risk of pulmonary embolis[243]. PE is currently the principal contributor to pregnancy-related deaths. During pregnancy, mortality rates with PE range from 0.9 to 2.1 per 100,000 patients have been reported in Sweden, Finland, UK and the USA [244]. In most cases, physiological changes happen, particularly during pregnancy, which predisposes patients to a higher rate of PE. These changes include pressure of the gravid uterus of pelvic and lower leg vessels, increasing stasis, a decrease in naturally occurring anticoagulants increased procoagulant plasma estrogen [245]. Typical PE symptoms are non-specific during pregnancy; dyspnea, tachycardia, and leg swelling are common presentations[246].

Imaging pathways utilised in this ED are often straightforward approaches. This local emergency department's protocol suggests that pregnant patients with suspected PE must go through a pre-probability for pulmonary embolism to identify the risk and need further imaging assessment. One of the issues is that the D-dimer increases in the majority of the patients after the first trimester[247]. However, a negative D-dimer result is valuable as a means of ruling out PE in pregnant and post-partum[248], without the need for imaging and its associated ionizing radiation[249]. In the local setting, pregnant patients with intermediate or low suspicion for PE is suggested to avoid undergoing imaging despite their D-dimer reading level.

Where symptoms associated with DVT are present, ultrasound evaluation of a low extremity is conducted. If the ultrasound is positive, then treatment is commenced, which is similar for DVT and PE. Where the ultrasound is negative, a chest x-ray should be used as an initial imaging modality. When the chest is normal with a high pre-test probability, doctors prefer to use a low

dose CTPA since it has fewer non-diagnostic scans, high specificity, and high sensitivity compared to a V/Q scan

CTPA offers high diagnostic accuracy for PE, as well as alternative diagnoses and lowers foetal dose depending on gestational age[250]. However, CTPA does come at the expense of higher maternal radiation exposure and breast dose and initiates concerns about developing breast cancer or the lifetime possibility of cancer. Moreover, the rate of suboptimal examinations is higher among pregnant patients. The physical changes of pregnancy cause tachycardia - fast heart rate and variable ventricular ejection rate. The latter is associated with low contrast volume and escalates the possibility of non-diagnostic CT scans. Therefore, this article highlights methods and techniques to decrease radiation dose and non-diagnostic studies in pregnant patients without affecting image quality.

6.2.3: Method

The number of pregnant patients undergoing CTPA is quite low. Therefore, to assess the low dose protocol's applicability in the dose and suboptimal scan in pregnant patients, this study was conducted using 9 case review series. All patients had an improved 80kV CTPA with tube current modulation with standard deviation level 8 (commercial name ‘Sure Exposure 3D’) and an effective mAs 258; the reconstruction algorithm used was FC 51 with lung window. Patients were asked to undertake a gentle breath-hold with their mouths open. A shorter delay time of 3 seconds was utilised between injection and scanning to overcome variable and swift contrast filling because of pregnancy's physiological tachycardia. A well-secured 18g cannula with a high flow rate (5ml/s) was used with a standard 50ml saline flush to decrease failure. Finally, patient education was conducted on breathing techniques with active coaching and relaxation techniques; gentle breath-hold with an open mouth at the time of the scan was used to decrease the Valsalva effect and motion artefact.

6.2.4: Findings

Nine case review series were included in this study. This case review series found that the radiation effective dose associated with a low tube voltage of 80kV protocol in pregnant patients ranged between 1.02mSv to 0.4mSv with a mean effective dose of 0.72mSv. It also found a higher contrast enhancement with the tube voltage of 80kV. The pulmonary trunk's maximum and minimum contrast enhancement was 640 HU and 320 HU, respectively, with a

mean contrast enhancement of 402 HU. This is a substantial improvement when compared to the prior standard protocol; out of nine patients, eight had good imaging quality, a single patient had satisfactory imaging quality, but imaging was affected by a respiratory artefact; this is visually demonstrated in table 6.5

Table 6. 5: Radiation dose and findings of the patients.

No	weight(KG)	age	HU	dose in (mSv)	Findings	Image Quality
1	78	28	401	0.8	There is no pulmonary embolus	Diagnostic image quality
2	91	32	331	1.02	There are no filling defects identified	Diagnostic image quality
3	89	34	350	1	There is no pulmonary embolus	Diagnostic image quality
4	76	27	640	0.51	There is no pulmonary embolus	Diagnostic image quality
5	82	35	402	0.78	There are no filling defects identified	Diagnostic image quality
6	72	33	411	0.7	No evidence of pulmonary embolus is seen	Diagnostic image quality
7	67	25	381	0.4	There is consolidation in right lower lobe.	Diagnostic image quality
8	85	38	320	0.71	There is no pulmonary embolus	Diagnostic with minor motion artefact
9	78	31	387	0.61	No evidence of pulmonary embolus is seen	Good image quality

6.2.4.1: Discussion

6.2.4.2: Radiation Dose Consideration in Pregnant patients

When patients are suspected of having a PE, imaging plays a crucial part in the diagnosis; this section will discuss imaging modalities' role.

Ultrasound is used to diagnose a DVT; it is fast, simple and has no ionising radiation but is often not available after hours. Nevertheless, the Royal Australian and Zealand College of

Radiologists notes that ultrasound is found to be negative over 90% of the time among pregnant women with suspected PE[96]. Thus, the college's advisable approach is not to use it as a first-line imaging modality except where they experience signs and symptoms associated with DVT[96].

Chest x-ray enjoys a significant role in the initial diagnostic imaging assessment for PE in pregnancy; it is used to avoid the necessity for further imaging by revealing an alternative diagnosis, primarily acute respiratory illness, such as pneumonia or pneumothorax. Major advantage of chest x-ray is low radiation dose (0.06 to 0.25 mSv)[97].

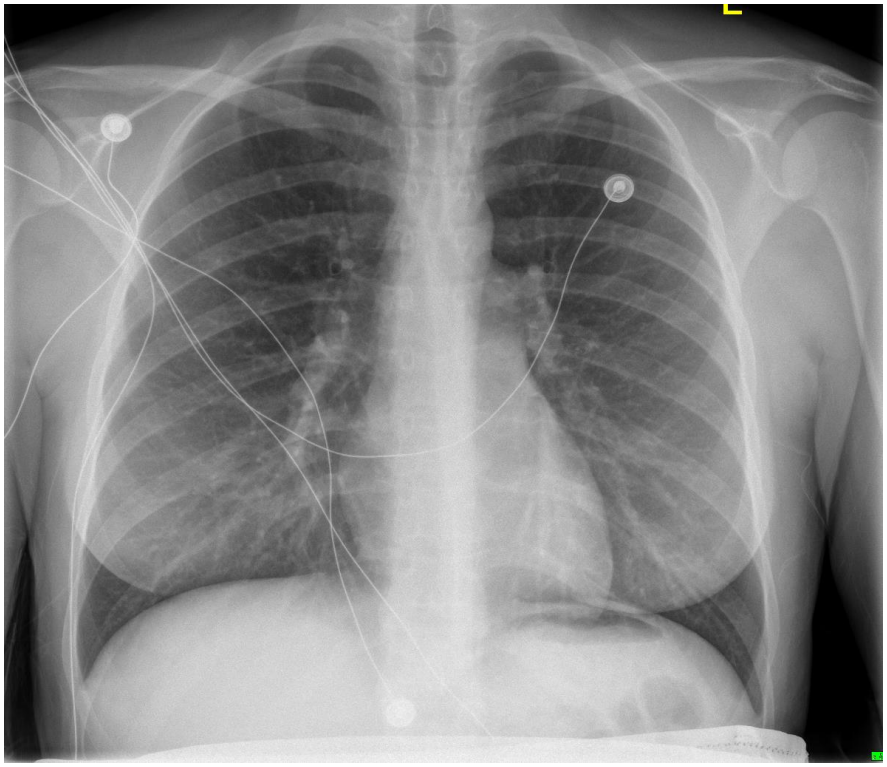


Figure 6. 8: Normal chest x-ray in of patient presented with pleuritic chest pain with tender calf.

Magnetic resonance angiography (abbreviated as MRA) is an appealing alternative imaging modality to CT for the examination of PE, especially in pregnancy, because it involves no ionising radiation. However, MRA has a high percentage of inconclusive findings, motion artefact, poor opacification, and more imaging and limited capacity to diagnose subsegmental branches or alternative diagnosis[97]. Before adoption into common clinical practice, further advances in technology and techniques is required.

V/Q scan can be described as a non-invasive technique of assessing the patency of pulmonary circulation. It utilised ionising radiation in the form of radionucleotide. Overall it is

regarded as one of the most important imaging modalities for PE. Nevertheless, a VQ scan is often inconclusive and difficult to interpret, necessitating further examination with CTPA when there is a high clinical probability for PE [92]

In the literature, the whole body's effective radiation dose and fetal dose were (1.2 to 6.8mSv) and (0.1to 0.8mSv) respectively[97].

A low dose CTPA is a favoured imaging modality when imaging for PE in pregnancy. Its primary merit over other modalities includes the capacity to illustrate alternative diagnoses contributing to the symptoms. CT is definitive in the majority of the instances and has higher diagnostic accuracy. Using a lower radiation dose of less than 1mSv is possible, as illustrated in figure 6.9. The whole body's effective radiation dose and fetal dose are about 0.8 mSv and 0.01mSv, respectively.

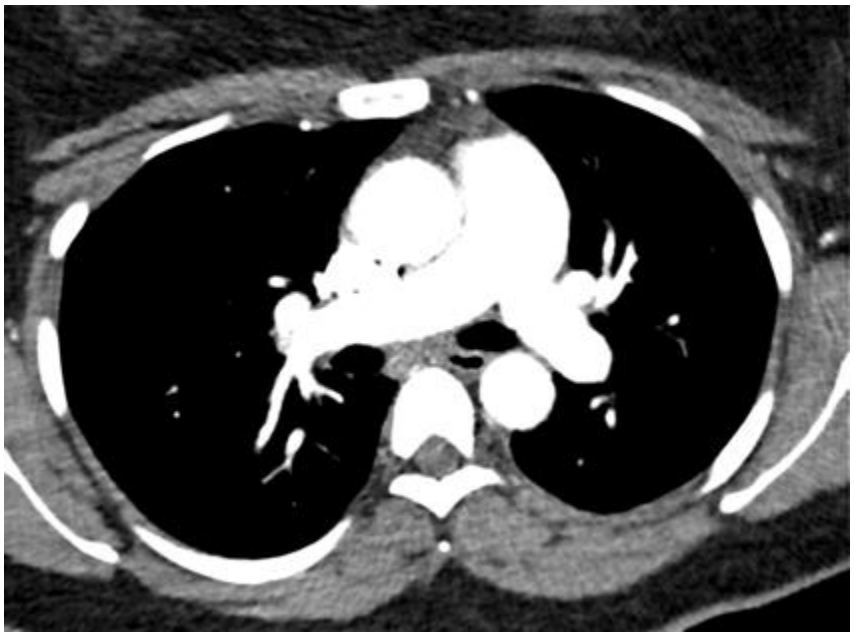


Figure 6. 9: Low dose CTPA scan for a 21-weeks pregnant patient. The radiation dose was 0.8 mSv. Contrast in the aorta due to fast heart rate of pregnancy.

CT imaging is conclusive in the majority of the instances and has higher diagnostic accuracy, which can diagnose or exclude PE in minutes. However, training staff performing CT on ways to decrease radiation is essential as well as having low dose protocols available for pregnant and young patients.

6.2.4.3: Foetus Risks in CTPA Study

As the foetal dose is CTPA is low because of distance from the imaging area of interest, it is thought that CTPA causes no quantifiable increased risk of foetus mortality or developmental abnormalities due to radiation exposure[251]. Schwartz et al. (2017) report that the American National Council Radiation Protection takes account of the radiation abnormalities negligible at less when the radiation dose is less than 50mGy when considering other risks in pregnancy. Advice from the Royal College of Radiologists and College of Radiographers in the UK states that CTPA has an approximate typical fetal dose of 0.001mGy, with the possibility of suffering cancer during childhood estimated at 1 in 1,000,000. Therefore, radiation exposure was considered negligible compared to the risk of PE [251]. Nonetheless, it should be stressed that whilst the risk is low, it is not zero and becomes important at the population level. Thus it is essential to maintain the radiation as low as reasonably possible.

The following table 6.6 discusses the limitation and strengths of CTPA and VQ scan imaging.

Table 6. 6: V/Q scan and CTPA strength and limitations.

CTPA	V/Q scan
Strengths are CTPA is broadly present in emergency departments. It consumes less than ten minutes to conduct the assessment. It generates sharper images that may reveal emboli in the segmental, lobar, and main pulmonary arteries. Medical doctors may easily detect diagnosis PE or other alternative diagnoses, for example, aortic dissection and pneumonia. Besides, CTPA offers a lower foetal radiation dose compared to V/Q scanning that is 0.003 to 0.131 mGy to that of V/Q that offers 0.32 to 0.74 mGy during the initial trimester via the pregnancy's third trimester[252]. **Limitation** It is risky among patients allergic to Iodinated contrast as well as those suffering from severe renal impairment with an eGFR of less than 30. It also has a higher radiation dose than V/Q scan to the beast.	The primary benefit of a V/Q scan is a low radiation dose than the standard CTPA. Female patients that have radiosensitive breast tissue may acquire a lower radiation dose than CTPA. CTPA investigation results in higher radiation dose breast tissue, typically 10-70 mGy vs< 1.5 mGy for the V/Q to breast[253]. However, the radiation dose to the lungs and uterus is higher for V/Q scanning, according to latest study[254]. Besides, it is safe for patients suffering from severe renal impairment and allergic to iodinated contrast with a GFR of less than 30. **Limitation** It is unable to detect any alternative diseases, for example, malignancy and aortic dissection. It is also not suitable for hemodynamically unstable patients because of cardiac failure or massive emboli since it needs up to 30 minutes to the assessment. Access and reporting after hours are limited. Besides, its diagnostic accuracy may be weakened where the initial chest X-ray reveals abnormalities, making CTPA the recommended imaging modality among these cases.

The main advantage of CTPA is it is easy to detect PE or other alternative diagnoses, for example, aortic dissection and pneumonia. However, using dose optimisation techniques are essential for young and pregnant patients.

6.2.5: Methods to Reduce Radiation Dose in Pregnant Patients

An improved 80kV CTPA protocol is the most appropriate method of decreasing radiation dose in pregnant patients. The advantage of such protocols lies not only in the lower dose but also in improved vascular enhancement, which reduces suboptimal examinations

Another alternative to decrease the radiation dose among pregnant women is using volume scanning. There is limited experience at this centre with volume scanning. It has been utilised in some clinical settings for non-pregnant patients. It revealed satisfactory image quality but whilst radiation exposure was reduced by 30% compared to the standard 100kV helical scan.

An 80kV helical protocol used in this study offers better image quality, greater radiation dose reduction and coverage of the entire lung fields to allow alternative diagnoses.

An extra method to decrease radiation dose is to decrease over-scanning during CT examinations, leading to a high radiation dose among patients with suspected PE without an improved diagnosis.

In my own calculation, when the scanning length was decreased to only 5cm, the mean effective dose was reduced on average by 18%. When scanning pregnant patients, the upper abdominal organs and lung apex are often excluded from the assessment since it may result in radiation dose in the absence of offering any important diagnostic data. The correct scan range is visually demonstrated in figure 6.10.

This local imaging department uses a lead apron to further reassure patients regarding radiation dose protection for the unborn baby. Shielding a radiosensitive baby is essential, achievable, and does not conceal the scan's desired area of interest. At this centre, breast shielding is discouraged since it is associated with some disadvantages, such as increased image noise and streak artefacts that impact the examination's diagnostic accuracy[162].

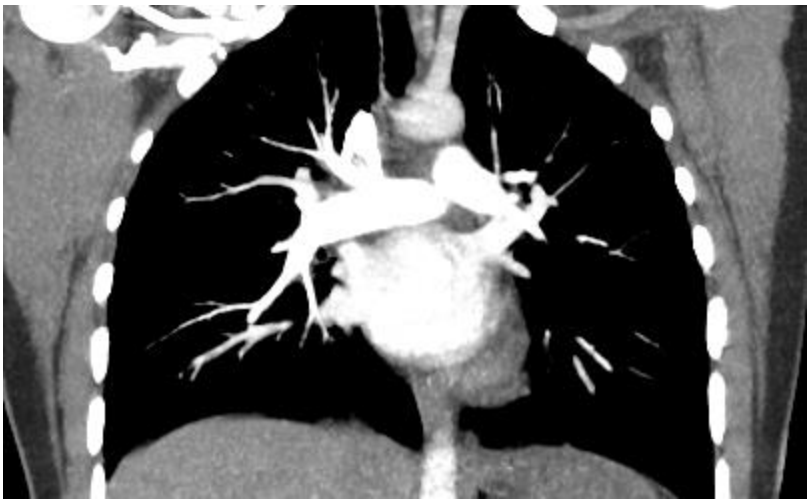


Figure 6. 10: A low dose of helical CTPA for a pregnant patient. The radiation dose is considerably decreased 0.61mSv due to reduced scan length.

Decreasing scan length is an effective way to reduce the mean effective dose but is often ignored by the imaging team.

6.2.6: Strategies to Decrease Failure Rates in Pregnant Patients

As mentions previously, suboptimal CTPA scans can increase particularly during pregnancy because of tachycardia. My local experience with utilised the noted prior techniques has helped us attain zero failed or suboptimal scans in pregnant patients for more than one year by reducing the common contributors to CTPA suboptimal scans, namely inadequate cannula Valsalva and tachycardia.

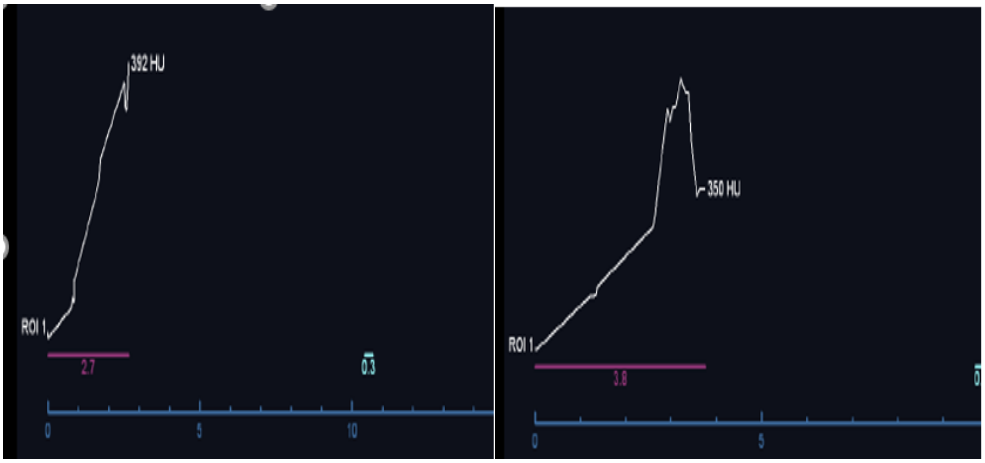
Tachycardia results in variable ventricular ejection leading to low contrast volume and enhancement. In pregnancy, during the scan, the monitoring slice at the pulmonary trunk reveals a high contrast enhancement; however, the contrast bolus has often passed through the pulmonary truck during the scan, which leads to low contrast enhancement on the pulmonary tree resulting in non-diagnostic examination.

The Valsalva effect is often initiated with the deep inspiration breath-hold, which leads to the contrast diluting in the pulmonary tree resulting in suboptimal images.

In the majority of the occasions, motion artefact, Valsalva, poor contrast enhancement and tachycardia may be reduced by educating patients. For example, patients were provided with appropriate breathing instructions, relaxation teaching and coaching to attain a gentle breath-hold with mouth open; the latter decreased tachycardia and Valsalva effect. A shorter

delay time (3 seconds vs standard 5 seconds) is important, as illustrated in figure 3, since the images contrast enhancement goes over 350 HU in less than 3 seconds of contrast injection (figure 6.11).

Further improvements to overcome suboptimal examinations can be a high rate of injection (such as 5 ml/s) and using a secured 18-gauge cannula in the cubital fossa flushed that has been flushed with 10ml saline to enhance and maintain the contrast flow rate during the entire examination. Less contrast volume can also be achieved through a saline bolus chaser with a double-barrel injector.

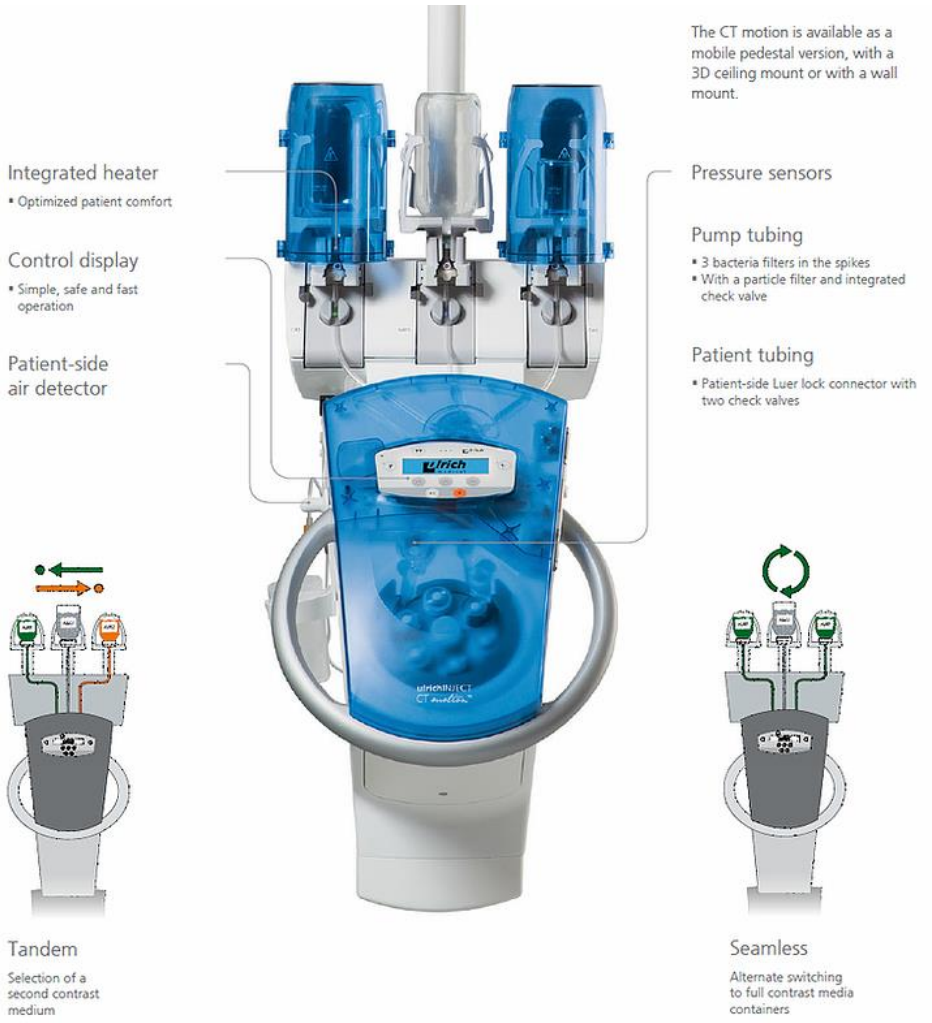


a b

Figure 6. 11: Contrast enhancement which quickly reached high HU less 3-second .image (a) at 392HU and image (b) 350HU.The ideally delay time is 3 seconds in pregnant patients.

Appropriate breathing instructions, 80kV, a gentle breath-hold with mouth open and a shorter delay time (3 seconds) are useful in decreasing Valsalva in patients with tachycardia.

An effective and superior injector apparatus such as a double-barrel injector can further reduce the cannula failure rate; this is illustrated in figure 6.12 with the ‘Ulrich’ brand of an injector. This type is used locally and equipped with 18 ml saline testing and can change both flow and pressure during contrast administration. This can be used to decrease suboptimal imaging and contrast extravasation.



Source: Ulrich Medical, used with permission, https://www.ulrichmedical.de/en/products/contrast-media-injectors/ct/ct-motion/[255]

Figure 6. 12: Ulrich double Barrel Injector can decrease suboptimal images, extravasation, and contrast volume.

'Ulrich' brand of an injector has 18 ml saline testing and the capability to change both flow and pressure during contrast administration; this is proven to decrease suboptimal imaging and contrast extravasation.

6.2.7: Conclusion

Whilst it is important to avoid unnecessary imaging of pregnant patients, it is often required in high-risk patients. When imaging pregnant patients with the above-noted techniques for low dose CTPA, this study demonstrated both reduced radiation dose and suboptimal scans in pregnant patients without compromising image quality.

6.3: Section Three: Validity and Reliability of the Protocol

When a new protocol is initiated in imaging departments, it is important to assess the protocol's consistency and accuracy. The low dose CTPA has been evaluated for 12 months in a busy emergency department in the Australia Capital Territory. To further extend the applicability of the low dose protocol, the aim of this section is to assess the validity and reliability of the protocol. This research project utilised a retrospective review to assess the strength and credibility of the low dose CTPA.

6.3.1: Method

A retrospective review involving a sample of 100 participants who underwent a low dose CTPA was conducted. The participants were selected randomly. Imaging assessment was conducted by extracting information from a picture archiving communication system to test the validity and reliability of low dose CTPA.

Patients were allocated to the low-dose CTPA protocol with the 'AID 3D Strong' image reconstruction process and a standard deviation of the tube current level 8 (Tradename: 'Sure Exposure 3D'). An effective mAs of 258 and tube voltage of 80kV with tube current modulation were utilised. A reconstruction algorithm utilising a kernel FC51 was utilised to provide reduced noise. To assess the validity and reliability of the low dose protocol; this study evaluated the number of PE diagnosed as well as the number of studies with suboptimal images, reduction in radiation dose, image enhancement, number of missed diagnoses and whether any patients returned for further assessment as a result of missed diagnosis.

The images were considered suboptimal or non-diagnostic when contrast enhancement was less than 210 HU in the main pulmonary artery or when the reporting radiologist graded the images as non-diagnostic or suboptimal. In the case of inadequate reporting or unclear statements, images were reanalysed, and a consensus was reached between the original report and the view of the reporting radiologist.

6.3.2: Findings

In this research project, five patients were discovered with positive PE. A total of seven patients were found to have had repeated CTPA within 12 months after the initial scan; one of

these patients was found to have a PE while the other six patients had alternative diagnoses such as atelectasis, infection, pulmonary fibrosis, metastasis, pulmonary oedema and emphysema.

With regards to suboptimal examinations, three patients were found to have minor suboptimal imaging; two of these cases were a result of the respiratory motion artefact. The other patient had low opacification of subsegmental pulmonary artery branches; a definite cause was not identified; the clinical significance of this is uncertain given it is subsegmental. The examinations were diagnostic to identify or eliminate PE and evaluate other acute pathologies that may present acutely or in the emergency department setting.

With regards to radiation dose reduction, the current low-dose CTPA maintained the considerable radiation dose reduction reported in chapters 5 and 6 without compromising the quality of the image. The mean effective dose was 1.14mSv, which is less than half the lower radiation dose than the 100kV standard CTPA protocol in the article two study. The radiation dose should have been lower as radiographers were required to restrict the range of scanning and avoid scanning the upper abdominal to decrease radiation exposure more, but this did not always occur.

Contrast enhancement was found to be 54% higher compared to the standard protocol. Mean contrast enhancement was 647HU and was greater than that of the standard protocol, 351 HU, as mentioned in the previous article two/chapter 6 study. Table 6.7 illustrates radiation exposure, contrast enhancement and objective image quality of radiologists.

Table 6. 7: A retrospective review involving the radiological findings of 100 CTPA cases.

No	Radiation dose (mSv)	Image Quality (HU)	Repeats in 10 months	Summary of Radiologist findings	Subjective Image quality
1	1.3	673	No	There is right lower lobe PE	Good
2	0.99	545	No	Pleural effusions /collapse/consolidation.	Good
3	0.74	539	No	No PE	Good
4	0.72	513	No	No pulmonary emboli were visible.	Good
5	1.47	524	Yes. 2 R	No evidence of PE, but had emphysema	Good
6	1.4	652	No	No pulmonary embolus	Good
7	1.2	361	No	Atelectasis/ left pleural effusion.	Good

No	Radiation dose (mSv)	Image Quality (HU)	Repeats in 10 months	Summary of Radiologist findings	Subjective Image quality
8	1.68	720	No	No pulmonary embolus identified.	Good
9	0.89	790	No	There is no pulmonary embolus	Good
10	1.3	657	No	Bilateral emphysematous changes. NO PE	respiratory motion artefact
11	1.16	509	No	No acute pulmonary thromboembolism.	Good
12	1.2	640	No	No PE	Good
13	0.99	626	No	No pulmonary embolus detected.	Good
14	1.2	740	No	No PE detected.	Good
15	0.63	727	No	There are no filling defects identified	Good
16	1.05	695	No	No pulmonary embolus identified.	Good
17	1.3	456	No	No evidence of pulmonary embolus is seen	Good
18	1.3	606	No	No PE	Good
19	1.2	676	No	Solitary pulmonary nodule	Good
20	1.3	563	No	No PE	Good
21	1.5	810	Yes. 2 Repeats	No PE. Infection only	Good
22	1.4	552	No	No PE	Good
23	0.68	758	No	No PE in a good CTPA study.	Good
24	0.98	705	No	Atelectasis	Good
25	1.2	452	No	NO Filling defects identified	Good
26	1.16	560	Yes	Metastases only identified.	Good
27	0.82	938	Yes	Pulmonary fibrosis.	Good
28	0.93	593	No	No PE	Good
29	1.2	603	No	No PE	Good
30	1.3	926	No	No PE	Good
31	1.3	324	No	Pulmonary embolus identified.	Good
32	0.96	348	No	No PE	Good
33	1.2	346	No	No PE	Good
34	1.19	750	No	Infective/inflammatory process.	Good
35	1.2	808	No	Metastases	Good
36	1.3	519	No	Atelectasis	Good
37	1.3	921	No	Extensive pulmonary embolus	Good

No	Radiation dose (mSv)	Image Quality (HU)	Repeats in 10 months	Summary of Radiologist findings	Subjective Image quality
38	1.02	935	No	No PE	Good
39	1.5	511	No	No PE	Good
40	0.75	1017	No	Metastases	Good
41	1.2	626	No	Bilateral pulmonary emboli	Good
42	0.96	861	No	infectious/inflammatory process	Good
43	1.3	420	No	No PE	Good
44	1.5	640	No	Pulmonary edema	Good
45	0.7	606	No	No PE	Good
46	1.4	672	No	Pulmonary nodules	Good
47	0.7	798	No	Consolidation	Good
48	1.2	722	No	No PE	Good
49	1.4	611	No	No PE	Good
50	1.2	624	No	Lymphadenopathy	Good
51	1.5	348	No	No pulmonary emboli.	Good
52	1.2	388	No	No pulmonary emboli.	Good
53	1	457	No	No emboli are seen	Good
54	1.4	1067	No	No emboli are seen	Good
55	1.1	875	No	Left pleural effusion	Good
56	1.4	642	No	4 mm solid appearing nodule	Good
57	1.4	369	No	Pneumonia.	Good
58	1.1	736	No	Atelectasis and small pleural effusions.	Good
59	0.57	1295	No	Emphysema with basal atelectasis.	Good
60	0.98	1014	No	No PE	Good
61	1.3	607	No	Primary breast malignancy	Good
62	0.96	783	No	No PE	Good
63	1.4	546	Yes	No pulmonary embolus identified.	Good
64	0.75	391	No	No evidence of a pulmonary embolus.	Good
65	0.96	907	Yes	Large pulmonary emboli. 2) PE follow up I mSv	Good
66	0.96	665	No	Pulmonary oedema	Good
67	0.94	532	No	No PE evident.	Good
68	1.1	577	No	No PE	Good
69	0.5	840	No	Bilateral effusions.	Suboptimal opacificatio

No	Radiation dose (mSv)	Image Quality (HU)	Repeats in 10 months	Summary of Radiologist findings	Subjective Image quality
					n subsegm. branches
70	0.56	472	No	No PE	Good
71	1.4	633	No	No PE	Good
72	0.98	703	No	No PE	Good
73	1.4	562	No	No saddle embolus or filling defect	Good
74	1.5	484	No	Bibasal moderate atelectasis	Good
75	0.8	673	No	No PE evident.	Good
76	1.6	813	No	No pulmonary embolism.	Good
77	0.98	578	No	Mild emphysema change	Good
78	1.3	713	No	Emphysematous change	Good
79	0.5	737	No	No evidence of pulmonary embolus	Good
80	1	852	No	lung mass	Good
81	1	425	No	No evidence of PE	Good
82	1.4	641	No	Negative study for PE.	Good
83	1.4	534	No	Bilateral lower lobe collapse / consolidation	Good
84	1.5	436	No	No evidence of pulmonary embolus	respiratory motion artefact
85	1.5	503	No	No evidence of a pulmonary embolus	Good
86	0.58	796	No	Enlarged subcarinal lymph node	Good
87	1.3	468	No	Negative study for PE.	Good
88	1.3	650	No	Bibasal rounded atelectasis.	Good
89	1.3	406	No	There is PE filling defect	Good
90	1.4	931	No	There is evidence of emphysema	Good
91	1.4	837	No	No pulmonary embolus	Good
92	1.2	640	No	No evidence of acute pulmonary embolism.	Good
93	1.09	731	No	Atelectasis	Good
94	1.2	461	No	Infection	Good
95	1.2	990	Yes Interstitial Oedema	Consolidation	Good

No	Radiation dose (mSv)	Image Quality (HU)	Repeats in 10 months	Summary of Radiologist findings	Subjective Image quality
96	0.8	629	No	Consolidation	Good
97	0.97	764	No	Pleural effusions	Good
98	1.4	616	No	No pulmonary embolus identified	Good
99	1.3	425	No	No evidence of acute pulmonary embolism	Good
100	1.49	412	No	Pulmonary nodule	Good

6.3.3: Conclusion

Radiologist consultant assessment feedback for the past 12 months and result from this validation concludes that this protocol is accurate and reliable and achieved the desired outcome. The original contribution to knowledge is that this study has found a new method that significantly reduces patient radiation dose and suboptimal examinations without compromising image quality.

6.4: Section Four: Strategies to Decrease Failure Rate and Radiation Dose on Larger Patients

Aim: This study's main purpose is to present a low-dose CTPA protocol to ensure that radiation exposure is as low as accurately possible without affecting the image quality and diagnostic utility.

As found in chapter four, a retrospective review of CTPA exams from picture archiving and communication system (abbreviated as PACS), there is an increased failure rate of CTPA among large patients and those with chest depth higher than 28cm. Suboptimal examinations were more frequent amongst patients with higher BMIs when utilising a 120kV scanning protocol.

A quality assurance assessment within this department has demonstrated that the number of suboptimal scans with poor contrast enhancement increased substantially among larger patients. Of the patients surveyed, 24% of the patients undergoing a 120kV examination had a suboptimal scan. This was concordant with previous work; Eyer et al. reported a high number of suboptimal examinations in patients with larger body habitus; this was one of the most significant contributors to non-diagnostic studies [29].

To improve the imaging of these patients, this imaging department ceased utilising the 120kV procedure. Two protocols were introduced, one for patients with larger patients between 100kg to 110kg and the other for patients between 110kg and 180kg.

The following review shows the implementation of new imaging protocols, which decreased radiation dose and suboptimal examinations.

6.4.1: Protocol One

In this study, larger patients weighing between 100kg to 110kg were allocated to the low-dose CTPA protocol with tube voltage of 80kV, image reconstruction process ‘AID 3D Strong’ and a standard deviation of the tube current level 6 (Tradename: ‘Sure Exposure 3D’). An effective mAs of 258 with tube current modulation was utilised. A reconstruction algorithm utilising a kernel FC51 was also used to provide reduced noise. A larger cannula with a higher injection rate of 5ml/s was required to increase the CT contrast enhancement. Finally, patient education on breathing with active coaching and relaxation techniques was provided to achieve a gentle breath-hold with an open mouth to decrease Valsalva.

Using this method permitted CTPA to be acquired with a considerable reduction in patient radiation dose, less suboptimal examinations, and higher contrast enhancement (Figure 6.13and figure 6.15). This technique's mean effective dose is relatively low at (DLP 88.10), which is 1.23 mSv; the image quality is also acceptable, as visually demonstrated in Figures 6.13 and 6.14.

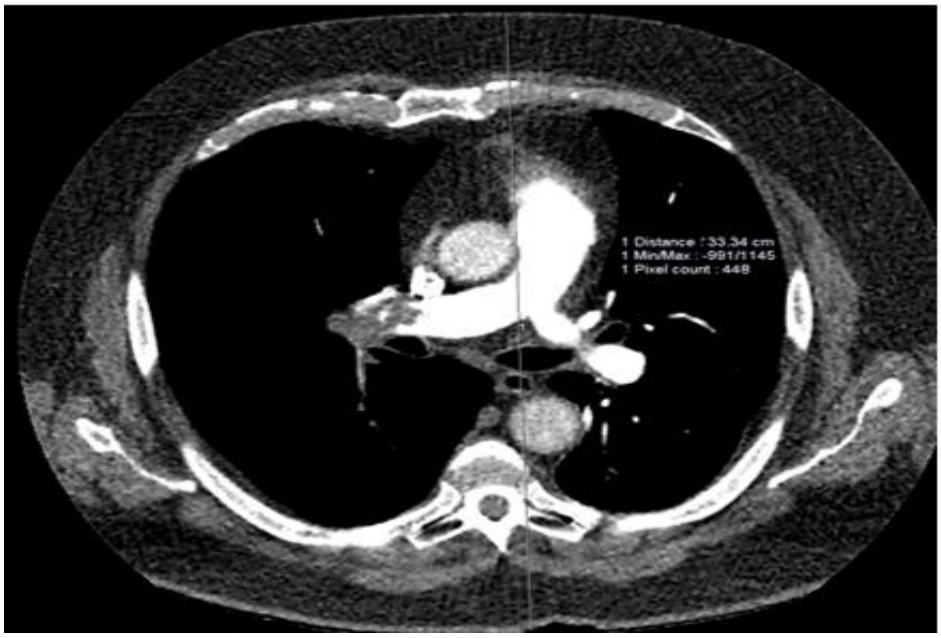


Figure 6. 13: A 67 years old large patient weighing 110kg. An effective dose of 1.23 mSv. PE partially occluded the right pulmonary artery.

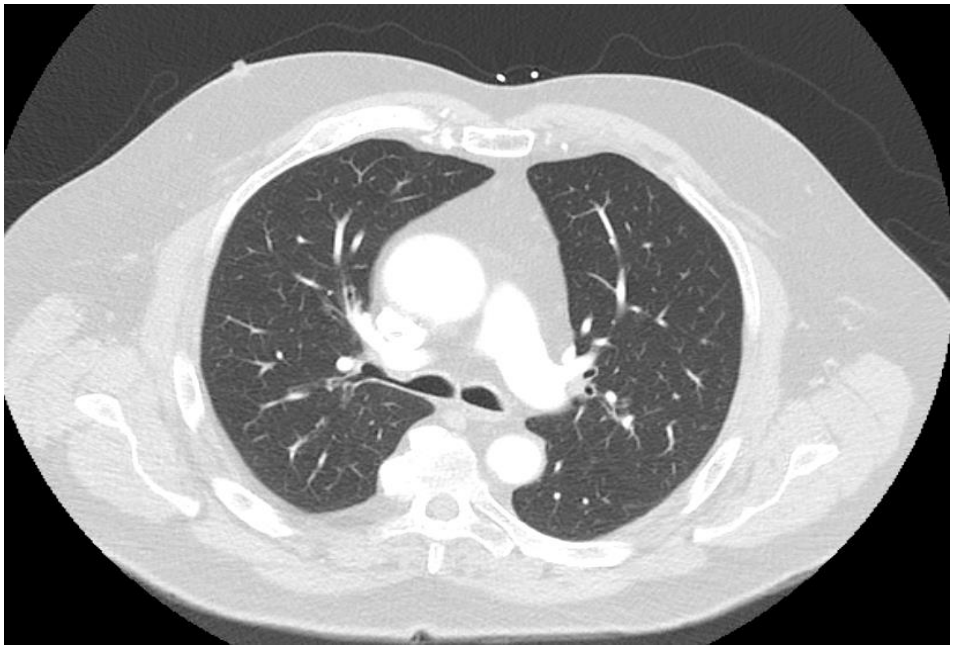


Figure 6. 14: The reconstruction kernel algorithm was FC51 with slightly reduced noises on the image.

Using tube voltage of 80kV, ‘AID 3D Strong’ and a standard deviation of the tube current level 6 permitted CTPA to be acquired with a substantial reduction while achieving improved contrast enhancement.

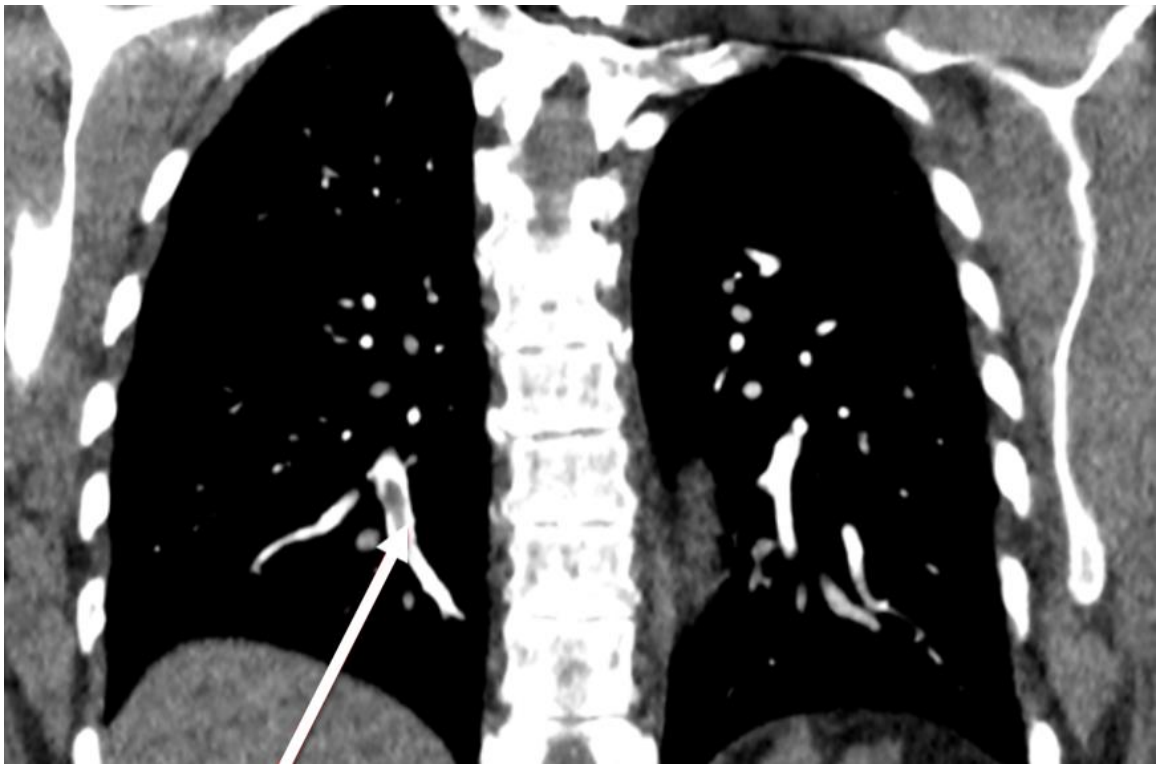


Figure 6. 15: Coronal image shows 108 kg patient, the red arrow shows PE filling defect of PE. The effective dose was 1.14mSv.

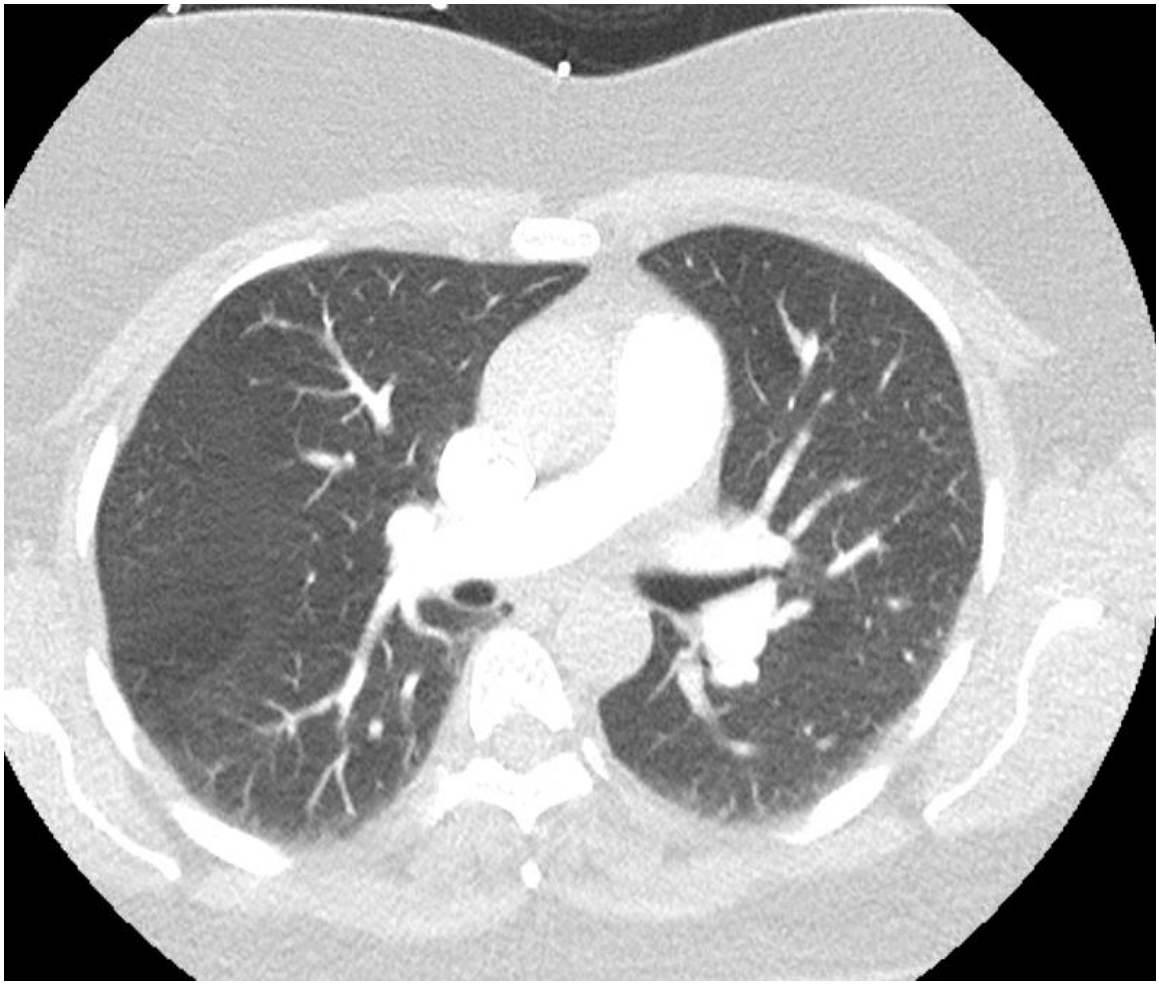


Figure 6. 16: Axial lung window of the above study illustrates acceptable image quality.

This image was performed in the early phases of this research project; there is image noise. However, in the late phase of this study, we significantly decreased image noise while adjusting the effective tube current or scanning time.

The following diagram shows changes made to this improved low radiation dose protocol.

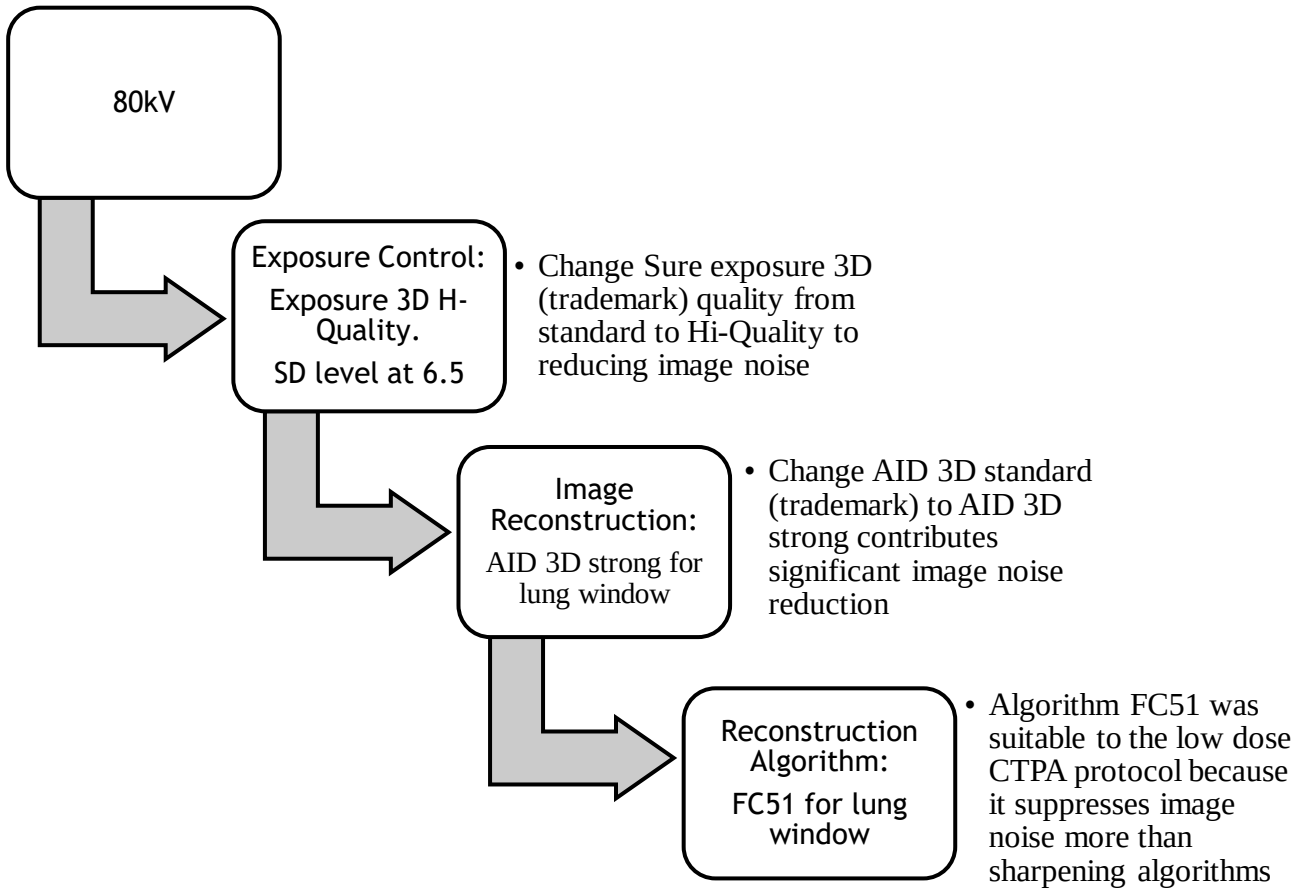


Figure 6. 17: Changes made to enhance image quality.

The above diagram shows changes made to enhance image quality in low radiation dose CTPA protocol.

6.4.2: Protocol Two Patients Weighing Over 110kg

For patients weighing above 110kg up to 180kg, this protocol used the same settings as the above protocol except the following. 1) Tube voltage was increased slightly to accommodate the patient size; patients were allocated to 100kV. 2) When patients weighed more than 140kg, scanning time is slightly increased, for example, from 3.2 seconds to 3.8 seconds, leading to increased effective mAs.

An 18G cannula with a higher injection rate of 5.8 ml/s was used with 70ml contrast followed by a 50ml saline flush. Patients were instructed to take a gentle breath-hold while their mouth is open to address the Valsalva. The breathing method has been effective and has decreased the Valsalva related suboptimal examinations as well as low contrast enhancement; this is visually demonstrated in Figures 6.18 and figure 6.19.

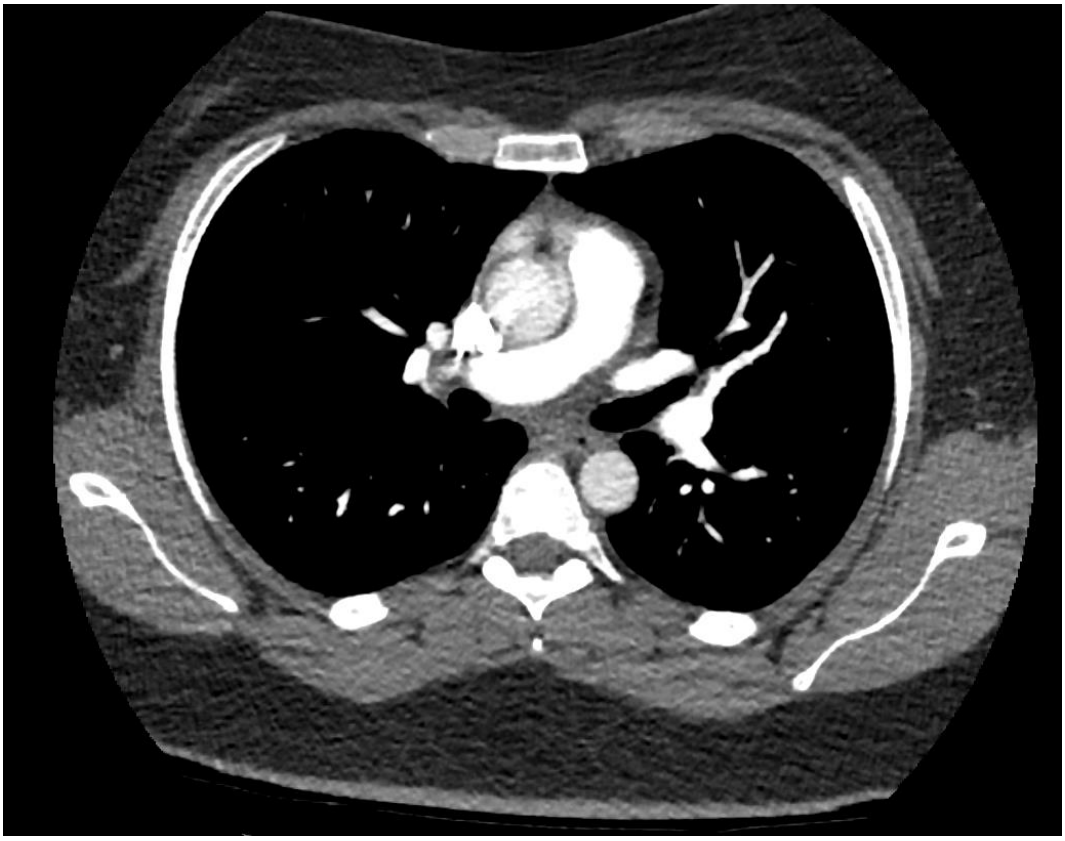


Figure 6. 18: An axial lung window of 135 kg patient, image with excellent contrast enhancement.

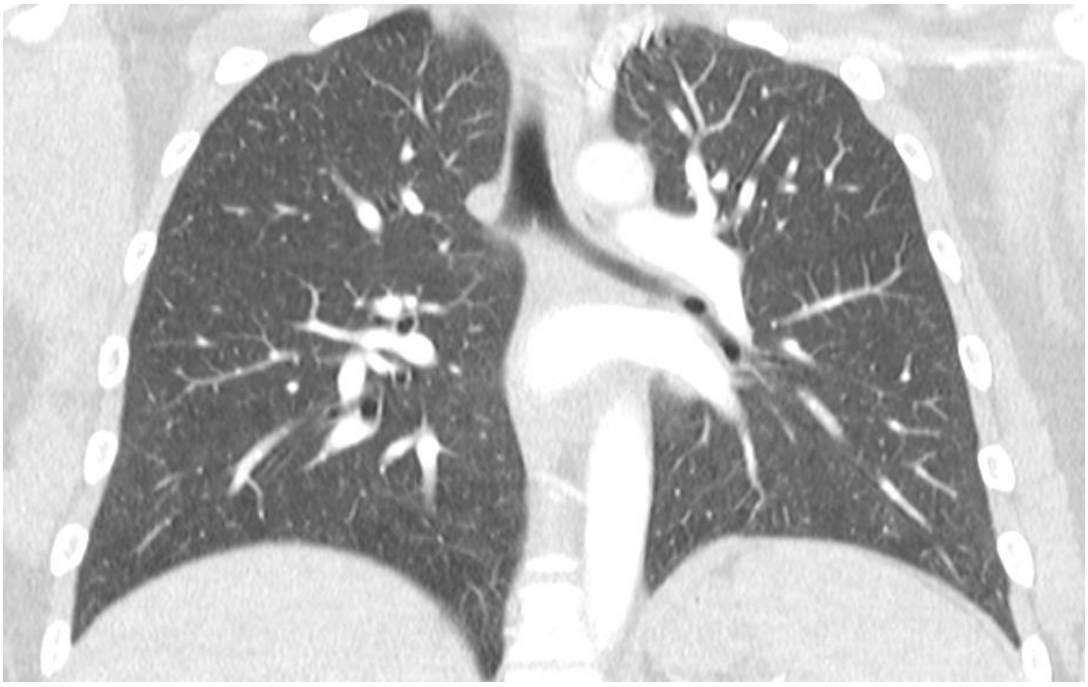
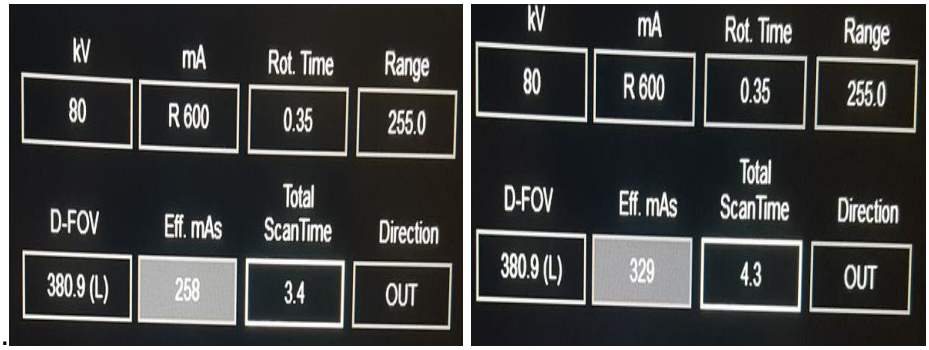


Figure 6. 19: Coronal lung window 135 kg patient, image quality can accurately diagnose or exclude PE and alternative lung diseases.

Using lower tube voltage and instructing patients to take a gentle breath-hold while their mouth is open addresses the Valsalva and decreases non-diagnostic studies considerably.

6.4.3: Total Scan Time for Larger Patients

Additional option to improve image quality and decrease image noise in patients at the higher end of each protocol (90-105kg and (140-180kg) was to decrease scan length by excluding a considerable portion of the upper abdomen and increasing scanning time, increasing effective mAs and reducing noise. Total scanning time was slightly increased at the maximum 1 second (as shown below figure from 3.4 seconds to 4.3 seconds). Subsequently, effective mAs was automatically increased from 258 mAs to 329 mAs.



a b

Figure 6. 20: Scanning time was increased by 0.9 seconds to decrease image noise. (a) Effective mAs was 258; scanning time was 3.4 sec. (b) The total scan time was increased to 4.3 seconds, and effective mAs was increased to 329.

It was found that the trade-off for reducing kV, decreasing scan length to area of interest whilst utilising low SD improved the image quality and ensured a significant reduction in image noise. Figure 6.20, in which total scanning is slightly increased, the patient's radiation dose was 1.2mSv, which is 45% lower compared to the previous 100kV CTPA of the same patient. Image quality was maintained and rate as good image quality without motion artefact.

6.4.4: Conclusion

This study confirms that improved breathing guidelines, venous access, higher injection rate, and utilising lower tube voltage improved contrast enhancement and reduced the likelihood of performing suboptimal examinations. It should be stated low contrast enhancement is usually high in large patients; however, these techniques decrease suboptimal examinations, even though other failures, including foramen ovale, can cause unpreventable suboptimal examination[256]

This research project suggests that medical imaging technologists should initially utilise an 80kV protocol for those with a maximum weight of 105 kg among larger patients with suspected PE. It is advantageous since the attenuation of iodinated contrast tends to escalate with the utilisation of a low tube voltage because of iodine's Kedge at 33 Ke. It was found that the 100kV protocol improved image quality and decreased radiation dose among patients weighing between 110 to 180 kg. Ultimately with larger patients, this department avoided utilising the 120kV since it generated sub-optimal images in the majority of the patients.

6.5: Section Five: Another Method of Reducing Radiation Dose is Volume Scanning

This section aims to briefly discuss other areas, such as volume scanning, which can lead to reduced radiation dose. The purpose of this section is to discuss the role of volume scanning in PE imaging.

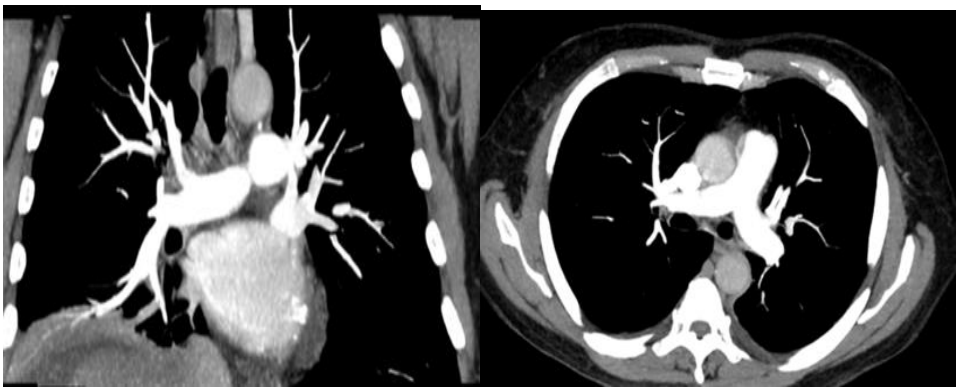
6.5.1: Volume Scanning

Volume protocols have recently become prominent in medical imaging departments due to the promise of reducing radiation and improving imaging and compliance. Volume scanning has been used in various areas, for example, shoulder, hips, vascular brain imaging, cardiac imaging, facial bones, and extremity. Currently, there is no literature available on CTPA volume scanning. However, in this study, a small number of patients (only 7) had CTPA volume scanning. They were allocated a low CTPA dose with a standard image reconstruction process AID 3D, an effective mAs of 258 and 100 kV, and a reconstruction algorithm-kernel FC 53 that has a tube current modulation.

Results from these scans reveal that volume scanning reduces radiation considerably. The maximum and minimum exposure were 1.6 mSv, and 0.76mSv, respectively, with a mean 1.2mSv. For example, in comparison to the helical scanning with a similar tube voltage of 100kV and exposure factors, the volume scanning decreases the radiation dose by approximately 30% or more (figure 6.24). The reduction of the radiation is a result of the short scanning time, which provides room for the new likelihood of utilising these applications where the length of the detector is increased to 25cm. Nevertheless, the present 320-slice system provides a volume scan with a 16 cm detector, and the entire length of the lungs cannot be scanned in most patients. This may miss pathology in lower lung lobes where volume scanning is used; the detector is visually demonstrated in figure 6.21. Volume scanning Images are also visually demonstrated in figure 6.22 and figure 6.23.

Volume scanning is ranked as the potentially effective technique for reducing radiation dose in CTPA but requires further research.

Figure 6. 21: A 16 cm PURE Vision detector in this scanner is capable of scanning a maximum of 16 cm area in one rotation.



a **b**

Figure 6. 22: Volume scanning displays optimal contrast opacification (b), lung base is not completely imaged due to the restriction of 16 cm detector row (a).

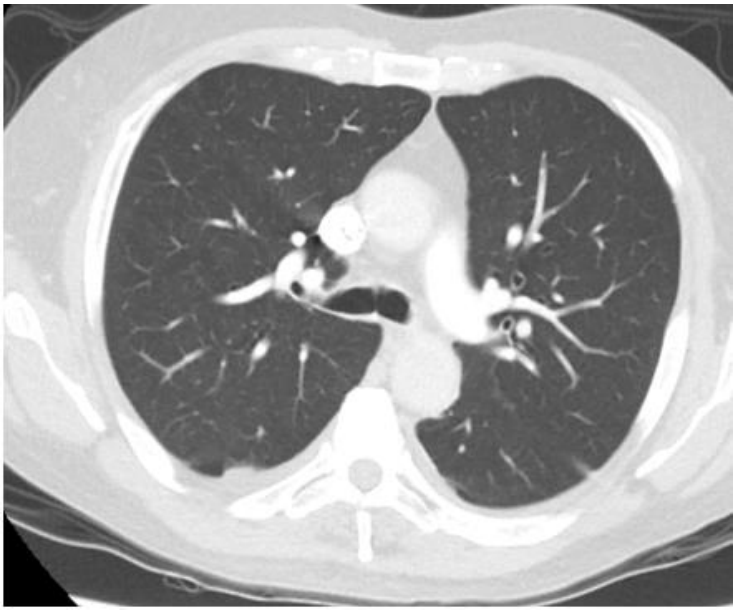


Figure 6. 23: Volume scanning axial lung window image displaying good image quality.

No.	Protocol	#of scan(s)	kVp	Range (mm)	Exposure Time (sec)	Body Size AP/LA	CTDIvol (mGy)	DLP (mGy.cm)
3	S&V	1	100	2.0	0.35	21.35/ 22.94	5.60 (Body)	1.10 (Body)
4	SURE Start	1	100	***	0.62	21.35/ 22.94	7.90 (Body)	1.60 (Body)
5	Volume	1	100	160.0	0.35	22.95/ 24.88	4.90 (Body)	78.50 (Body)

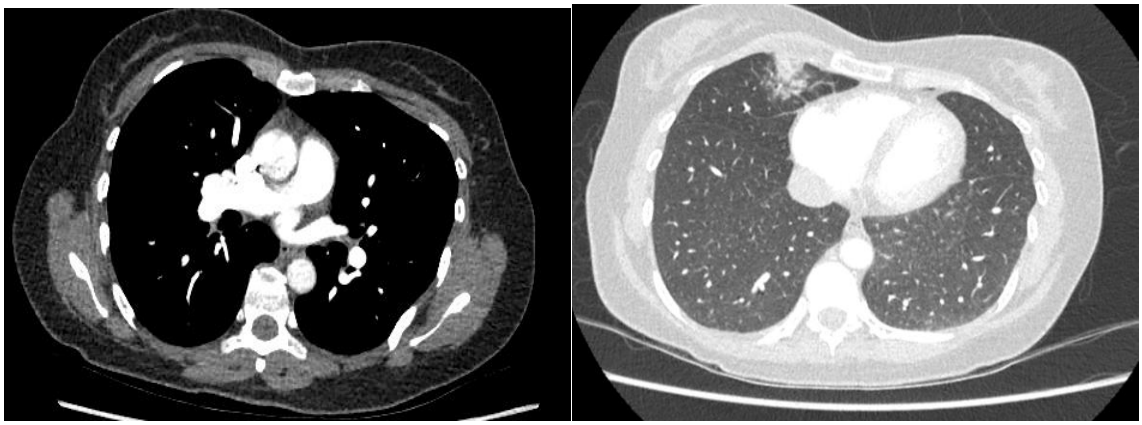
Figure 6. 24: Exposure utilised in volume scanning in 16 cm length.

The effective dose of the above case was 1.1 mSv. When the full length of the chest is scanned, the radiation dose would be expected to escalate more than the 80 kV protocol because of 100kV.

The following sections will discuss the further imaging role for 80kV helical protocol, which may not be achieved while using volume scanning due to a small 16 cm detector length.

6.5.1.1: *i)* Volume Scanning PE vs Pneumonia

The image in figure 6.25 shows optimal contrast opacification of the pulmonary arterial tree. There is dense pulmonary consolidation with air bronchogram consistent with subsegmental pneumonia, which causes the symptoms and could have been missed in 16 cm detector scanning.



a b

Figure 6. 25: Low dose protocol with lower lobe pneumonia consolidation, excellent image quality and low radiation dose of 0.7mSv achieved.

This is one of the reasons that I stopped using volume scanning as routine standard PE imaging as there are other alternative diseases in lung bases, and volume scanning is unsuitable in the emergency setting.

6.5.1.2: *ii)* Volume Scanning Aortic Dissection vs PE imaging

Another reason that volume scanning is not suitable in an emergency setting is that medical practitioners request CTPA to exclude PE as well as aortic dissection, as in the case figure 6.26 and 6.27. Imaging with helical 80kV is useful to exclude aortic dissection and provides a much larger scanning range than the 16cm provided by volume scanning.

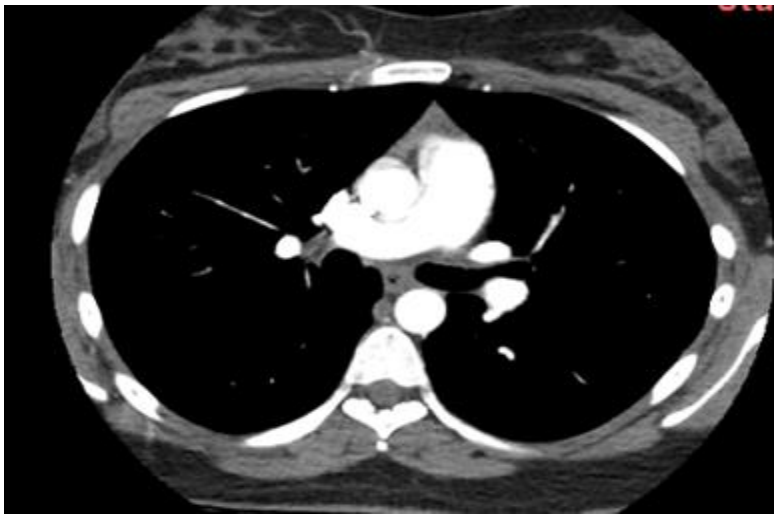


Figure 6. 26: A 20-year-old patient images with sudden-onset left-sided chest pain radiating to back tachycardia and hypertensive.

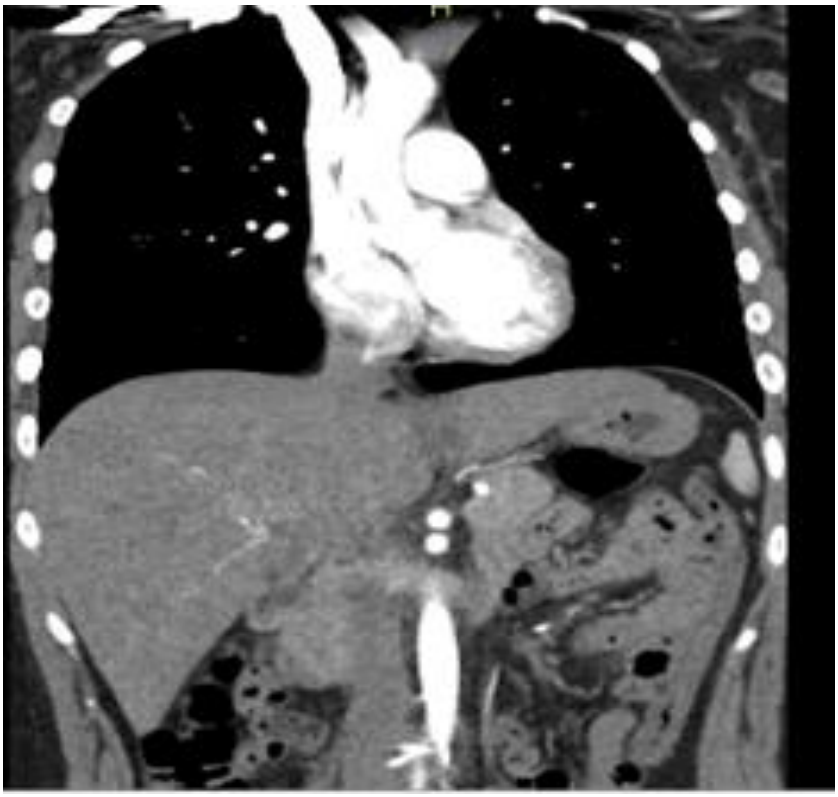
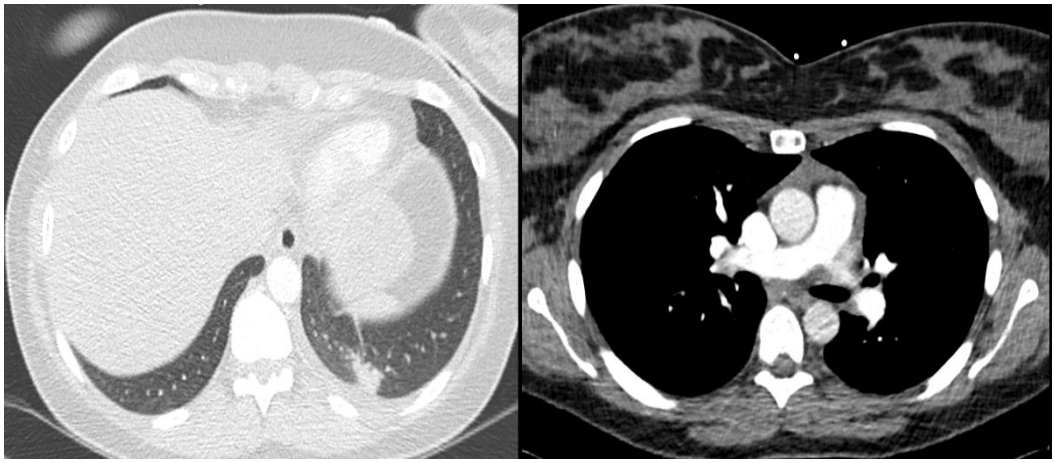


Figure 6. 27: Coronal images of the patients showing good image quality for aortic dissection imaging in the low dose protocol.

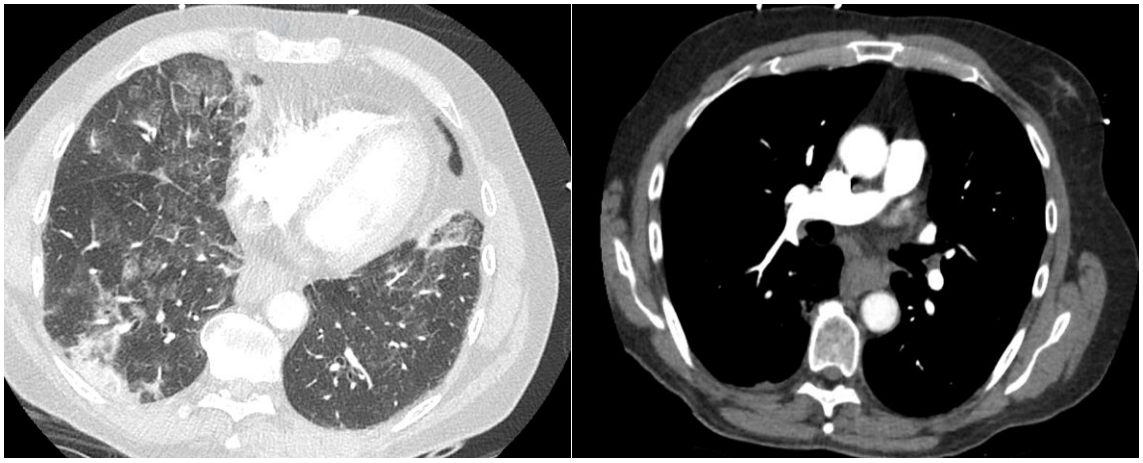
6.5.1.3: *iii)* COVID 19 Screening vs PE imaging

A further current situation that volume scanning is not suitable in the emergency setting is for coronavirus and PE imaging which requires imaging of the entire lung. With the current pandemic, the use of CT pulmonary angiogram increased in both the respiratory and emergency medicine settings, the reason may be that nasopharyngeal and saliva test is not 100% accurate, and imaging is utilised when there is a high clinical suspicion. This can be facilitated with the use of a low dose CT pulmonary angiogram to rule out the typical appearance of COVID 19 or potential PE. Complete lung assessment would not be proved by volume scanning, which would miss pathology in both the basal (figure 6.28) and apical lung areas



a b

Figure 6. 28: Lung window with a wedge-shaped area of opacity(a). The patient was presented with cough, chest pain, suspicion for COVID 19 or PE, had COVID swabbed. Image (b) shows low dose CTPA with good contrast enhancement.



a b

Figure 6. 29: An 80kV protocol CTPA, lung window with ill-defined patchy consolidation and ground-glass opacity typical appearance for COVID 19 (a), excellent contrast enhancement (b), no PE detected in this patient presented with cough, hemoptysis, tachycardia and raised inflammatory markers.

The typical appearance of coronavirus overlaps with other lung diseases such as viral pneumonia, organizing pneumonia, influence and acute interstitial pneumonitis. Typical changes include ground-glass opacification/opacity, consolidation, a crazy-paving pattern of changes and enlarged lymph nodes. Figure 6.29 demonstrates what is often the appearance of COVID 19 infection, namely consolidation and ground-glass opacity.

In summary, the helical improved 80kV protocol is suitable in an emergency setting. It can accurately demonstrate PE CT radiographic features, including filling-defect, and include Central: doughnut sign, railroad track sign, rim sign, and eccentric clot. Secondary findings included pleural effusion, atelectasis, and right heart strain, mosaic perfusion with reduced vasculature in lucent areas and infarct with peripheral opacity. It accurately demonstrates features that are common in PE differential diagnosis, including emphysema (CT characteristics include small round low attenuating that are equivalently distributed holes that have ill-described borders); Pneumonia (ill-defined patchy consolidation and ground-glass opacity) and atelectasis (typical features of a mass-like consolidation, it may demonstrate centrally located mass which obstructs bronchus)

Chapter 7: Discussion and Conclusion of the Thesis

The purpose of this chapter was to provide an in-depth discussion of the results. This discussion restates, evaluates, and interprets the results by going into detail about the meanings of the findings. The chapter suggests recommendations based on the result findings on radiation dose, suboptimal examinations and CT overuse.

This research aimed to offer a CTPA protocol that is suitable, accurate, and reliable with a low radiation dose without compromising image quality.

The main objectives of this study were:

1. To determine factors that contribute to CTPA overuse and explore ways to reduce over utilisation of CT pulmonary angiogram.
2. Create a low dose CTPA 80kV protocol while using adjusted tube current standard deviation and improved image reconstruction processing.
3. To determine whether the confidence in detecting pulmonary embolism with the novel CTPA protocol is acceptable to clinicians compared to the standard 100kV protocol.
4. To determine whether the novel CTPA protocol with gentle breath-hold with open mouth technique is effective for decreasing suboptimal CTPA examination in patients weighing below 105kg.

The current research found that an 80 kV CTPA protocol can be implemented clinically while providing good imaging quality and low image noise. The radiation dose was reduced significantly with the use of 80kV, lower standard deviation tube voltage, enhanced image reconstructions algorithm and extra image processing. The low dose protocol achieved an image quality that was objectively similar to that obtained with a standard 100kV CTPA protocol.

The research evaluated diagnostic confidence and found diagnostic accuracy equal to that of the standard protocol.

This study implemented and evaluated a new breathing technique in conjunction with the 80 kV protocol to reduce radiation dose and reduce the number of suboptimal studies.

The research explored the clinicians' opinions regarding radiation, radiation risk, image quality and the new CTPA protocol. Whilst it would be outside the scope of this study to

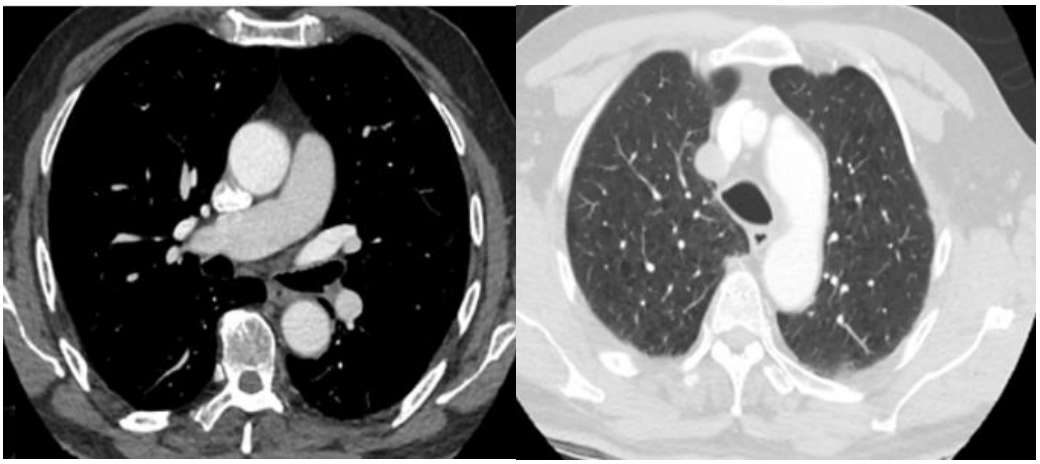
implement interventions for the findings regarding CT overuse, this study presented recommendations relevant to this clinical setting.

Overall the study accomplished its aim of decreasing the patient radiation dose as well as reducing the number of suboptimal studies. The outcomes of the research work are discussed in greater depth in the following paragraphs.

7.1: Section One: Radiation Reduction and Image Quality

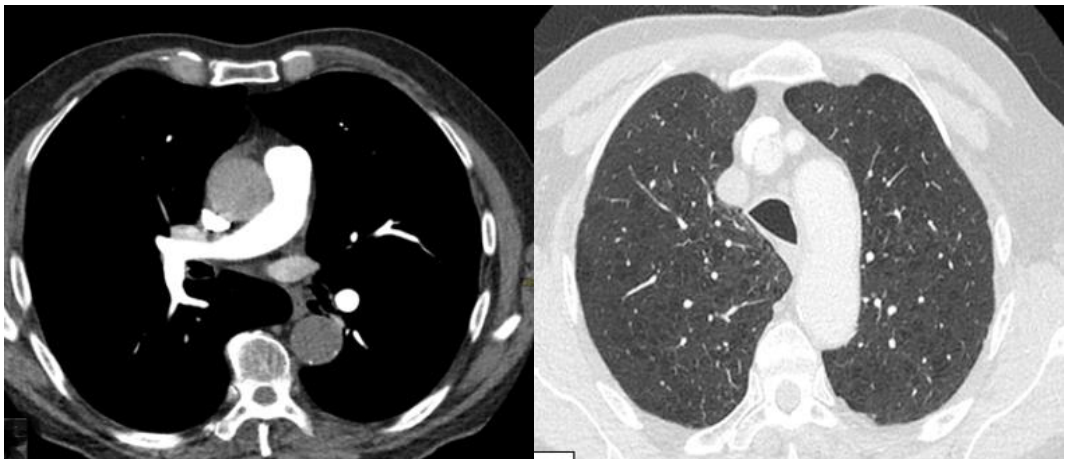
The research shows that there was a 66% reduction in the effective dose with a comparative study when using an improved 80kV protocol. The median effective dose was considered lower with the 80kV protocol than the 100kV protocol, 1.005 and 3.03mSv, respectively. In this study, the median effective dose was compared with diagnostic reference level (DRL) data from studies in other countries (Ireland, Switzerland and Malaysia); the dose is significantly lower (less than half) than other established DRL[14, 105,230]. Across the imaging departments, this protocol provides the lowest radiation dose available in imaging departments in Canberra and, most likely, Australia.

The radiologists subjectively found no significant variation between the image quality and diagnostic accuracy with the low dose protocol compared to the standard protocol. Furthermore, as analysed with the chi-square test, radiologists' objective image evaluations showed that the quality of CTPA with a low dose and standard 100kV protocols is similar for image quality and to diagnose or exclude pulmonary embolism. Figure 7.2 illustrates the low dose of CTPA image quality.



a b

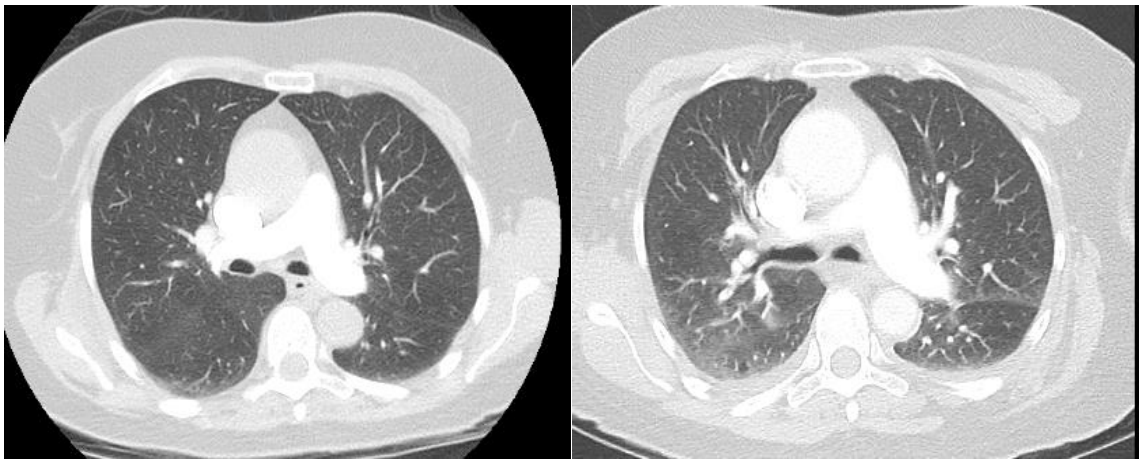
Figure 7. 1: The standard CTPA, with slightly reduced contrast enhancement (a). The radiation dose was high at 5.5 mSv. There is no evidence of PE. Moderate emphysema noted (b).



a b

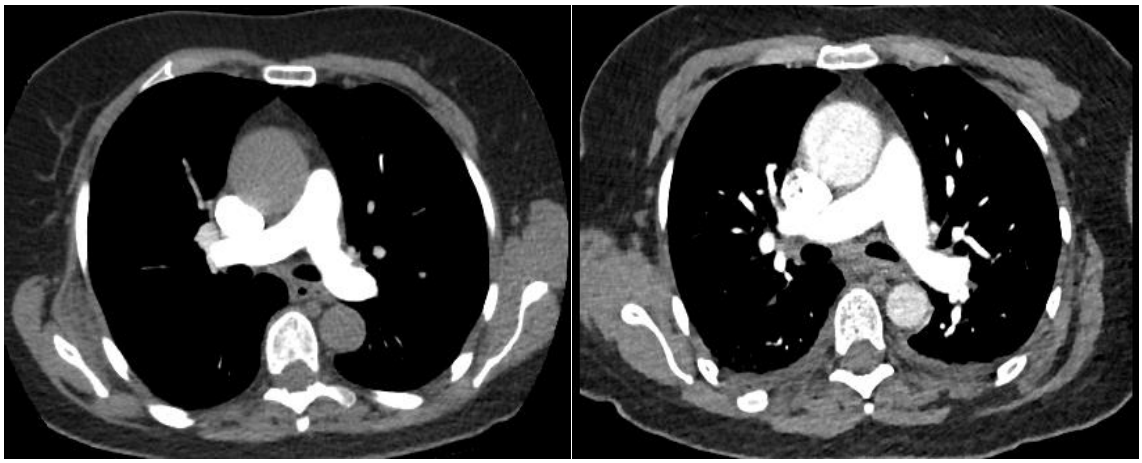
Figure 7. 2: Low dose 80kV CTPA of the same patient, with excellent contrast enhancement (a).Radiation dose at 1.4mSv.There is no evidence of PE. Moderate emphysema noted (b).

Though the research attained a significant decrease in image noise, even though there existed a small upsurge in the image noise, particularly and most evident in the patients at the larger end of the spectrum, the escalation in the image noise did not affect the accuracy of the diagnosis. Most of the patient's image quality was comparable, as illustrated in Figures 7.3 and 7.4 of the same patient who had CTPA in both 80kV and 100kV protocol. In this case, the improved 80kV preserved image quality while decreasing radiation dose from 2.8 mSv to 1.12 mSv.



a b

Figure 7. 3: Image (a) lung window of 80 kV, (b) lung window of 100Kv protocol.



a b

Figure 7. 4: Image (a) improved pulmonary arterial tree enhancement of the 80 kV protocol, (b) 100 kV protocol with comparable image quality.

This research also showed improved pulmonary arterial tree enhancement, which is another significant attainment of this protocol that decreased the possibility of a non-diagnostic scan; this is visually demonstrated in figure 7.4 (a). The improvement in the pulmonary arterial tree enhancement can be attributed to the low tube voltage tendency in bringing the photon energy near the iodine contrast K-edge 33.3, which raised the pulmonary arteries contrast enhancement. Therefore, detecting the pulmonary emboli filling defects within the contrast occupied pulmonary arteries became easier for physicians to identify and interpret images immediately as they are available. This improvement allows clinicians to quickly diagnose pulmonary embolism and decrease waiting time in the ED, which instils patient satisfaction.

Furthermore, in this improved 80kV protocol, it was possible to use the lowest volume of contrast medium while maintaining diagnostic quality (46mL). It is clearly advantageous in patients with a low glomerular filtration, patients with existing chronic kidney diseases and those with restricted intravenous cannula access who may profit from decreased quantity of contrast agent.

7.1.1: Further Optimisation

It is recommended medical imaging technologists are expected to decrease over-scanning and position patients correctly to optimise this new low dose protocol further.

In this regard, this research shows that reducing the scanning range is an effective technique of lowering extra radiation dose but is often ignored by imaging departments. A possible cause for over-scanning might be an attempt to ensure coverage of the lowermost lung bases, which can often be very low lying and not able to be imaged on a CTPA unless a considerable portion of the upper abdomen was imaged. A solution for this is to use a lateral scan tomogram for planning the CTPA.

Furthermore, patient centring is also a significant factor that affects the radiation dose among patients of various sizes. Incorrect patient centring simultaneously decreases the quality of the image and increases radiation dose as scanners are manufactured to be most effective with central positioning. Therefore patients need to be centred within the CT gantry for correct imaging, ideally using the sagittal laser positioning system.

During this study, it has been observed various CTPA cases where the radiation dose or the image noise appeared to be higher compared to the accepted dose limits and often de-centring was seen. Hence it is critical to ensure correct centring to radiation dose is as low as achievable.

7.2: Section Two: Suboptimal Exams

This research succeeded in reducing suboptimal examinations which were common in previously used standard CTPA protocols, particularly both 100kV and 120kV.

This was discussed in the suboptimal study two, chapter six, named ‘Approaches to reduce suboptimal CT Pulmonary angiogram for evaluation of pulmonary embolism’. The technique of gentle breath-hold with an open mouth and an improved 80kV protocol achieved an excellent contrast enhancement CTPA with lower suboptimal examinations and a considerable decrease in patient radiation dose without affecting the image quality.

Three contrast optimisation factors contributed to the improvement of the above achievement in decreasing suboptimal and non-diagnostic examinations.

7.2.1: Valsalva Manoeuvre

First of all, this study decreased the Valsalva manoeuvre, which common cause for suboptimal examinations. The study findings show various reasons why the Valsalva manoeuvre results in a lower contrast enhancement due to its effects on breathing mechanics, blood flow dynamics, and venous return to the heart. A deep inspiration breath-hold instantly prior to scanning caused intrathoracic pressure to compress the inferior vena cava and superior vena cava, leading to a reduction in cardiac filling and a fall in cardiac output. At the end of Valsalva, venous return into the right atrium increases. Overall, deep breath-hold disrupts contrast flow to the heart to a variable degree, thus unpredictably impacting the pulmonary arteries' contrast enhancement.

Historically medical professionals in imaging departments have been undertaking CT scans after an automated voice command for breath-hold. This method results in a considerable proportion of the scans having low contrast enhancement and being non-diagnostic. An alternative suggestion from some studies is to perform the scan at the end of expiration; this method may improve pulmonary artery enhancement; however, my findings from scans at the end of expiration show that this method produces poor image quality in lung windows which impacts diagnosing lung parenchyma diseases, this has also been reported in previous studies [171, 172]. In expiration scans, lung window images appear to increase lung attenuation and

decreases lung volume. This is often referred to as ‘spurious ground-glass changes’ and can be mistakenly diagnosed as infection such as COVID or pulmonary oedema, so this should not be used. A gentle breath-hold with an open mouth technique was utilised in this study, and this significantly decreased Valsalva related suboptimal examinations while increasing the contrast enhancement.

7.2.2: Injector Apparatus

Secondly, a superior injector apparatus with a saline bolus chaser from a dual-barrel injection was used; this effectively decreased the cannula's failure rate. The Ulrich injector is equipped with an 18 ml saline testing capacity and the ability to change the injection pressure rate during the contrast injection. Unlike past practice, saline testing is done while the patient arm is in a position that is to be used during the scan. In my experience, this markedly decreased suboptimal images, cannula failure and contrast extravasations. Saline testing and then changing arm position create problems in cannulas that are positional (positional mean cannula works in one position and does not in another position). A well-secured 18-gauge cannula in the cubital fossa @5ml/s is utilised to achieve an optimal flow rate.

Thirdly, in this research, an adjusted 80kV protocol was used. The rationale for this was to move closer to the attenuation coefficient of iodine. The increased contrast enhancement and reduced radiation dose were significant contributions that emerged from the context of this research project.

Other failures can cause suboptimal images, which will be discussed in the following paragraphs.

7.2.3: Motion Artefact

Motion artefact is the second leading cause of suboptimal imaging. It creates streaky shading that mimics pathology in the surrounding pulmonary structures. Motion artefact is a key problem, and it is driven by patients' capacity to hold their breath and patient motion. Being able to offer optimal diagnostic examinations is both protocol and patient dependent.

The ability of the patient to cooperate is essential in terms of suspending movement and breathing. This is significant in evading the occurrence of respiratory motion artefacts. Besides, motion artefact develops an inaccurate positive filling defect, mainly where the contrast

enhancement appears low. This restricts the radiologist's ability to diagnose precisely, usually in segmental and sub-segmental pulmonary arteries.

In some cases, radiologists may over-diagnose pulmonary embolism due to motion artefact creating an apparent filling defect in the artery. Such phenomena can also restrict a physician's capacity to identify the nature of a real pulmonary embolus and whether the filling defect is crucial, and if anticoagulation management is warranted or not. Moreover, this is a challenging issue for medical practitioners, and it must be recognised that anticoagulation medication carries a life-threatening risk of bleeding.

This study shows that in most instances, the motion artefact may be decreased through educating patients, such as providing appropriate breathing guidelines and teaching gentle breath-hold. Moreover, implementing a shorter scanning time with gentle breath-hold, using lower tube voltage to improve contrast enhancement and decreases the rate of indeterminate CT pulmonary angiograms.

It should be recognised that motion artefacts can remain unavoidable in a small number of severely ill or intubated patients who cannot cooperate with breathing guidelines.

7.2.4: High tube Voltage 120kV

This study ceased using the 120kv protocol because many of the scans under this protocol had low contrast enhancement or suboptimal imaging. Ending the high tube voltage protocol was important in medical imaging because it reduced patients who used to have high radiation exposure and inconclusive results.

Overall this study significantly decreased the leading cause of suboptimal exams, which was low contrast enhancement. While an effective solution has been implemented to decrease suboptimal and low contrast enhancement, there are still non-diagnostic studies in a small fraction of the patients in this imaging department. Technical failure, mainly cannula failure, causes a small percent of partial or complete suboptimal examinations. Concurrently motion artefact remains an issue in producing partially suboptimal imaging; this is also more marked in large body habitus patients and patients who are unable to cooperate with breathing instructions. Therefore, it is essential to acknowledge that this method fully achieved the intended target of

increasing contrast enhancement and attained the expended objectives of decreasing non-diagnostic and suboptimal studies.

In summary, having lower tube voltage, high injection and excellent venous access improve contrast enhancement within the sub-segmental pulmonary arteries as well as decreases the possibility of suboptimal examinations. Patients must adhere to breathing guidelines while attempting not to take a deep breath since they may result in Valsalva and recurrent scans.

7.3: Section Three: CTPA Overuse

This study's positive PE diagnosis was 11% lower than Sharma and Locus's study, ranging from 12.0% to 28.1%[10]. Canada also reported higher a positive PE rate of 17.8% and 15% in their emergency departments[11, 12]. This means that these imaging departments are scanning more patients than the above departments.

The best way to reduce radiation dose is to decrease the overall CTPA referral rate. Overuse can be reduced by addressing underlining issues such as time constraints, overcrowding, inadequately trained physicians, a lack of available hospital beds, and time pressures on clinicians, leaving little time for physicians to perform a precise examination and utilising pre-test probability tools centred on the history and physical examination. Throughout my discussions with clinicians, it was entirely agreed that probability testing and scoring systems effectively guide emergency physicians to improve diagnostic accuracy as well as patient treatment.

It is essential to decrease the number of CT referrals by accurately differentiating acute respiratory diseases from pulmonary embolism to avert a further increase in medical imaging radiation.

Clinical presentations remain the most critical feature that allows medical doctors to narrow down the differential diagnosis.

In pulmonary embolism, patients often have a short clinical history (unlike deterioration over a few days in pneumonia)

There may be a history of previous venous thromboembolism or risk factors such as recent surgery, recent trauma or immobilisation (such as a long-distance flight) causing haemostasis and a hypercoagulable state (e.g. burns, trauma, surgery, history of cancer/malignancy). Patients may have a history of recent DVT symptoms, such as a painful, red and swollen lower limb example or other risk factors such as hormone replacement therapy or taking the oral contraceptive pill. Important symptoms of PE include dizziness/presyncope, syncope, worsening shortness of breath, pleuritic chest pain (pleurisy is also common in pneumonia), DVT symptoms, reduced exercise tolerance and sometimes cough with haemoptysis. Haemoptysis is also common in bronchitis and in tuberculosis. Sometimes, the clinical examination may be completely normal; however, patients will often have a low-grade

fever (not high grade like in bacterial pneumonia), desaturation, and tachypnoea with increased breathing tachycardia and hypotension. Tachycardia, hypotension and shortness of breath are the most common that I have seen in patients diagnosed with PE. They may have a postural blood pressure drop (although this can also occur in infection). Clinically they may have an elevated jugular venous pulse, a parasternal heave or a loud P2 heart sound on auscultation, although these are not common. Usually, auscultation of the lungs is normal; however, if they have developed a pulmonary infarct from the PE, there may be a pleural friction rub or crackles on auscultation in the area of the pleuritic chest pain. The patient may have clinical signs of a DVT (unilateral swollen, tender and erythematous lower limb).

The ECG is most often normal but can show signs of right heart strain- sometimes, this may present as an S1Q3T3 sign (uncommon). There may be new right axis deviation, new right bundle branch block, anterior or inferior T wave inversion, or new atrial flutter/fibrillation.

Blood gases often show hypoxia with low paO2 in respiratory failure, low paCO2 from hyperventilation, but lactate is usually not elevated. Blood tests, including full blood count, biochemistries and renal function, are often normal. The CRP can be slightly elevated (not dramatically elevated as in bacterial pneumonia), but this can be markedly elevated if there has been pulmonary infarction.

A chest x-ray is often normal but, in rare cases, can show a Hampton's Hump sign or Westermark's sign (focal oligaemia in areas of thrombus involvement) or increased size of the pulmonary hilum from pulmonary thrombus impaction. Echocardiography can show signs of acute right heart strain and can sometimes visualise the thrombus and exclude other conditions (e.g. pericardial effusion). The gold standard of diagnosis is CTPA. In patients who are unable to have a CTPA (for example, contrast allergies/anaphylaxis, thyroid disease or severe renal impairment), VQ scan may be used [257].

D-dimer is recommended with patients with a low probability for PE prior to CTPA. The D-dimer may be elevated in pneumonia and other conditions (such as lung cancer, other malignancies and other haematological or inflammatory conditions). Consequently, that is why it is not a good test to rule out a diagnosis of PE, but it has a high negative predictive value and can be used for the exclusion of pulmonary embolism. For example, if a patient has a high fever, cough, dyspnoea over one week and the chest x-ray shows consolidation, a D-dimer test can

be performed, and if it is negative, it indicates it is highly unlikely for the patient to have PE, and the most likely diagnosis is pneumonia.

In this hospital, D-dimer is elevated at 0.5mcg/mL as per emergency doctors' survey; hence, elevating the d-dimer threshold to reduce unnecessary CTPA studies has been suggested[258]. Shifting the cut-off value from 0.5mcg/mL to 0.85 mcg/mL would significantly increase the specificity from 13% to 51% while maintaining the same sensitivity of 100%[259]. Hence, this study suggests a change in the d-dimer cut off value to that indicated in the above recent study.

It is challenging to distinguish between acute respiratory conditions and PE; sometimes, doctors can initially make a wrong diagnosis. Furthermore, some clinicians believe that even those who follow best practice guidelines are vulnerable to litigation. Consequently, fear of prosecution leads to unnecessary testing, and a significant number of exams are requested as a defence against a lawsuit, not necessary as a medical necessity. Over-utilisation to decrease vulnerability to litigation is a major issue in medicine. Preventable medical testing leads to wastage of valuable resources, increased radiation exposure, and escalates medical treatment prices among the patients. What is the solution? While I have no simple solution for this issue, some recommendation has been provided in the recommendation section.

7.4: Section Four: Limitation, Recommendations and Extendibility

7.4.1: Limitations

This research was conducted using qualitative and quantitative evaluations to investigate CTPA; as with most research, limitations are inherent in both the methods and insights gained. One of the research methods' most significant limitations is a reader may be biased towards lower dose imaging because the radiologists prefer brighter low dose CTPA images.

Other limitations are:

- The sample size was relatively small in the image evaluation survey and the pulmonary embolism differential diagnosis survey, both as a function of where the research was conducted and a limited number of questionnaires that were returned.
- The budget was another factor that is linked to the inability to evaluate a larger sample size in both image evaluation and surveys. This may restrict the generalisation of the findings.
- In the prospective comparison study, the minor difference between groups in terms of age, patients' weight and size may have a minor contribution to the measured differences. For example, the mean age of the participants in the control group A was 56.050±19.66 years, whereas this for the test group was 54.06 ±21.52. However, the difference is not significant in terms of patients' weight; the participants' mean weight in control group A was 69.88±14.23 years, whereas this for the test group was 68.96 ±13.45. It is anticipated if there was an effect, it would be minor.
- Ethics approval restriction was another issue with regards to pregnant patients presenting with tachycardia. The study intended to introduce a new adjusted scanning technique while using new volume scanning. In this protocol, the idea was to use an automated bolus tracking system formulated at 250HU with the region of interest (ROI) positioned within the pulmonary trunk and while using a decreased scanning delay time. Implementing this was not possible for two reasons. Firstly there were ethics approvals restricted to non-pregnant patients. Secondly, the 80kV protocol with the gentle breathing hold technique decreased the suboptimal studies significantly, and subsequently, there was no need to introduce a new technique in these patients considering the risk of technical failure.

- Regarding the Valsalva study, a budgetary limitation was a significant issue; this has led to the inability to collect data from the Valsalva study with MRI imaging further to define the impact of Valsalva on pulmonary arterial physiology. The MRI in the hospital is another department. Therefore, the cost of one scan to examine effects on breathing mechanics, blood flow dynamics, and effects on venous return to the heart was significant at $800 per patient. The feasibility evaluation indicated a minimum of 50 patients with a total cost of $40 000. As a result, this study limited the evaluation and substituted echocardiography assessment with cardiology and a smaller number of patients as a case study only.
- There was an issue with accessibility to an appropriate emergency consultant to further understand their views on CT pulmonary angiogram over-ordering. Over-ordering is not a preferred discussion in the emergency department, and it was hard to approach in follow up interviews. A small number of radiologists in this imaging department may limit the generalisation of the findings.
- It is significant to note that the study did not get the desired result in the patient centring experiment. Incorrect patient centring decreased the quality of the image while simultaneously increase the radiation dose. On preliminary CT phantom tests, fluctuating results were seen, and therefore, it was not possible to continue this test due to the initial results' inconsistency.
- Over scanning was a significant issue that restricted the ability to achieve the desired radiation exposure reduction. This is because the imaging team is attempting to ensure coverage of the lowermost lung bases, which can often be very low lying and cannot be imaged unless a large portion of the upper abdomen is scanned.

7.4.2: Research Recommendations

7.4.3: Future Research Recommendations

Volume scanning reduces radiation considerably (by almost 30% in comparison to helical scanning) with similar exposure factors. The reduction of the radiation is a result of the shorter scanning time. In this study, a small study number of patients had volume scanning under the 100kV protocol; it is anticipated that using improved 80kV will significantly further decrease radiation dose; however, this requires further investigation. There is a need to conduct further study on 80kV volume scanning in pulmonary embolism imaging, particularly in imaging departments that have 640 slices scanners.

Researchers investigating the 80 kV volume scanning may need to work with CT system engineers with experience in algorithms, detectors, and image noise reduction software to explore the volume scanning protocol further, not just in reducing radiation dose but also in reducing noise and enhancing image quality. Enhancing image quality by using new dose reduction software, algorithms, and adjusted standard deviation with increased affective mAs may make the 80kV volume scanning protocol more attractive than the current protocol.

Further areas for exploration are:

- Additional research on the image quality image and a further lessening in suboptimal images and image noise are required among large patients undergoing the current protocol.
- Much more research is needed in CT overuse, appropriately designed research on the impact of CT overuse on radiation dose and its cost. This will further enable us to implement additional evidence-based policies that can reduce CT overuse.

7.4.4: Recommendations for Medical Doctors

It has been noted that there is little formal training based for doctors on radiation harms and safety. It is recommended to increase medical radiation awareness by performing teaching sessions that would benefit physicians and enhance their radiation awareness and patient safety.

Furthermore, it would be recommended to emphasise clinicians to use improved evidence-based guidelines, appropriate use criteria for CTPA and V/Q scans, and pre-test probability based on the physical and history investigations (such as the Geneva score or Wells) in combination with the D-dimer test.

Wells score, a score below two, represents a low likelihood for PE and of two to six indicate a moderate chance while a score of over six shows a high probability for PE. The problem that can cause CTPA overuse in emergency departments is that using one clinical feature in Wells criteria (heart rate>100 beats/min which is score 1.5 plus PE is likely or more likely than alternative diagnosis (score 3) can give you a moderate chance of having PE (score 4.5) which warranties CTPA. I recommend using all other clinical features first, and using PE is likely or more likely than an alternative diagnosis as a last resort.

Also, D-dimer is elevated at 0.5mcg/mL in this hospital as per the emergency doctors' survey. Elevating the d-dimer threshold to reduce unnecessary CTPA studies is essential. Shifting the cut-off value from 0.5mcg/mL to 0.80 mcg/mL would increase the specificity and decrease the increasing number of CT pulmonary angiograms. The lowest D-dimer level with positive PE was 0.84 mcg/mL in the retrospective review. The above changes would probably improve patient assessment accuracy and further decrease CTPA overuse.

This study shows that most doctors fail to provide adequate information on radiation dose and the risk associated with the scan. It is recommended that clinicians and the healthcare team as a whole inform patients of the risk linked to radiation exposure. Patients should have adequate as well as honest communication regarding their care. It is recommended to educate patients and empower them to make appropriate medical decisions in their imaging and treatment planning.

7.4.5: Recommendations to Health Care Providers

Overcrowding is a significant issue in the emergency departments in the Australian Capital Territory; it is influenced by many factors: the most important is the overall number of patients, medical doctor availability, and the number of beds accessible in the emergency department. To address the overcrowding, this hospital is expanding the number of beds accessible to the emergency department; an extra 22 new treatment spaces will be added. It is also hoped that patients will be able to be seen faster as the emergency departments expand. The expansion may not solve the entire issue, but it will definitely ease overcrowding and waiting times. Therefore, I recommend increasing medical doctors and hospital beds to reduce pressure on staff and increase patient satisfaction. In doing so, doctors will have more time to accurately undertake pre-test probability centred on the physical and history examinations, and patients will receive better and safer patient care.

7.4.6: Recommendations for State Government

Whilst medical doctors are working to the best of their practice, they sometimes miss PE diagnoses, which leads to malpractice and complaints.

It recommended that the state government should more explicitly express that medical and other staff will be protected from potential unfair legal issues. State governments should initiate an honest discussion about the risk involved in patient care, including the possibility of missing diagnosis. Patients should understand that medical practice is not always 100% accurate despite doctors' best efforts, and sadly, mistakes in clinical assessment do happen. Hence when an error occurs, setting expectations and preventing similar mistakes are essential. Furthermore, implementing better guidelines with evidence-based appropriate imaging pathways and consensus with the input of emergency consultant doctors, radiologists, and the patient representative is necessary to protect doctors from potential unfair lawsuits. Medical doctors should be indemnified from risks for understandable mistakes that arise from clinical assessment or interpretation of the studies. The risk may be able to be covered by personal indemnity insurance or state government recognition of that risk in their indemnity coverage. Both of these steps are unlikely to change significantly either.

7.4.7: Recommendations for Imaging Departments

Imaging departments should ensure that each radiation exposure is justified. Patients should have minimum radiation exposure required to achieve the intended objective of diagnosing or excluding pulmonary embolism. This is achievable by optimising imaging protocol while using methods of this study or doing other radiation reduction methods in consultation with medical physicist and CT applications team.

This study recommends imaging departments to utilise this new enhanced low dose protocol or similar protocols; it is also essential to reduce over scanning to decrease extra radiation dose.

Furthermore, the imaging department should regularly and consistently monitor exposure to patients. Having radiation dose recorded in the medical records and available to medical doctors each time clinicians are requesting new scans is also suggested; this is recommended to increase doctors' awareness and reduce unnecessary imaging in patients who have had multiple imaging exams and presentations.

7.4.8: Recommendations for Patient

Patient education on radiation dose is essential. The patient should be given sufficient information and opportunity to understand the potential benefit of CTPA as well as the risk of radiation exposure. Patients should question how much radiation exposure they will receive from the CT examination, what will happen if they do not get the CT pulmonary angiogram and the availability of any radiation-free alternative imaging modalities that could be substituted. If CT is the only available option, as in the case of this hospital, then patients should get a radiation dose that is the lowest as possible in their cohort.

7.4.9: Radiation Risk versus the Benefits

While it's essential to reduce over-ordering of CTPA, it is vital not to hesitate to undergo a low dose CT scan when patients are at high risk of PE with a positive D-dimer. Early diagnosis is vital for effective PE management and outweighs the risk of radiation exposure. However, the dose optimisation measure discussed below should be employed routinely to decrease radiation dose.

Imaging departments should utilise dose reduction techniques to ensure the radiation dose provided to patients is maintained as low as possible without compromising image quality to attain an accurate diagnosis. When CT imaging is necessary, radiation dose should be decreased as low as possible in order to diagnose or eliminate pulmonary embolism and alternative diseases.

Clinicians should reduce the number of CT referrals while adopting the principle of radiation exposure rationalisation. They should ensure the examinations are clinically indicated, and there should be a net benefit for the patient linked to each CTPA study conducted. Fear of legal repercussions should ideally not be considered while making clinical decisions.

Radiation exposure control is another idea that effectively addresses radiation exposure, in which patients should not exceed accepted yearly or lifetime radiation exposure limits. Overall, radiation exposure reduction could be achieved by decreasing the number of CT orders and using radiation in a manner as low as achievable to diagnose or exclude pulmonary embolism such as that provided by the new low CTPA protocol.

7.4.10: The Validity and Accuracy of the Protocol

The new low dose CTPA protocol is accurate and reliable. Radiologists from this hospital have reported using this protocol for the past 14 months; over a thousand patients underwent this protocol and found no difference in diagnostic accuracy between the low-dose protocols and the previous standard 100kV protocol.

Furthermore, a sample of 100 participants who went through a low dose CTPA was selected and assessed to test protocol validity. This assessed image quality, the number of missed diagnoses, and whether any patients returned for further assessment due to missed diagnosis and no statistical difference was found.

Furthermore, this assessment found that seven patients had repeated CTPA within ten months of these; one patient had followed up imaging for a positive PE, while the other six patients had alternative diagnoses such as atelectasis, infection, pulmonary fibrosis, metastasis, pulmonary oedema, and emphysema. No patient returned for further examinations as a result of a missed diagnosis. In objective image quality evaluation, this study found image quality and diagnostic accuracy of the low-dose protocol is equivalent to that of the standard 100kV protocol.

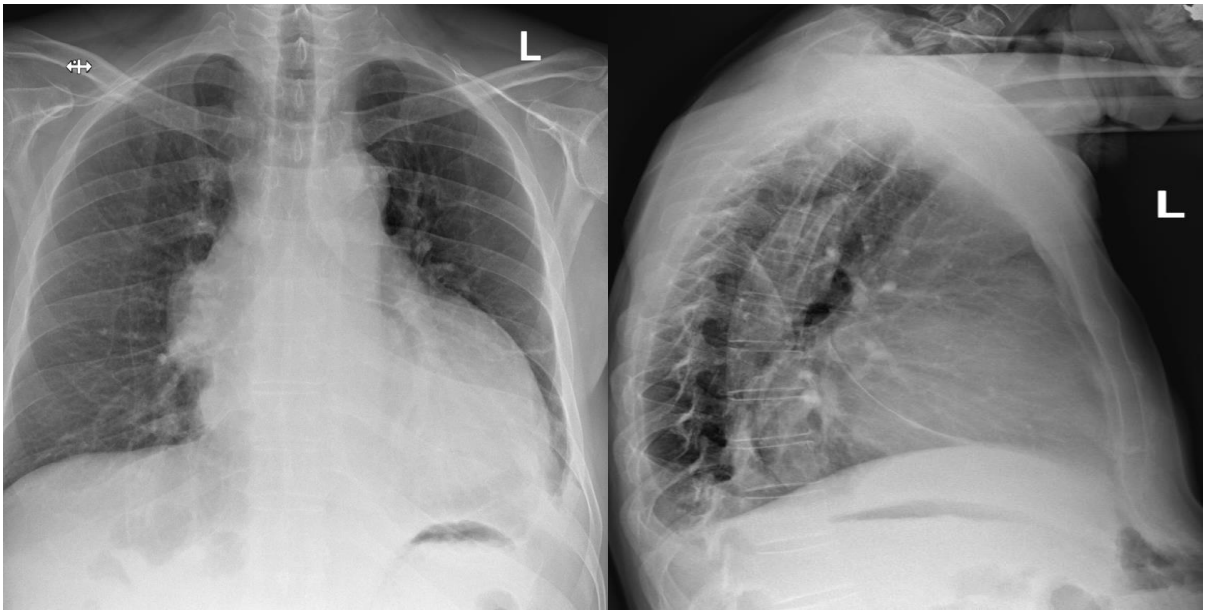
Because CTPA is the most commonly utilised test for pulmonary embolus, another assessment method against diagnostic quality was not available. Pulmonary MRA is not utilised at the facility, and VQ scans are neither commonly conducted nor comparable to CTPA. The protocol has been tested on an adequate number of patients in varying groups and has shown consistency similar to the old protocol.

7.4.11: Extendibility of This Protocol

The impact of the low dose protocol and technique is not limited to CTPA alone. The low dose protocol can be extended to other areas, such as imaging aortic dissection in patients weighing less than 105kg. During this study, this imaging department started using this protocol when doctors requested aortic dissection scans while at the same time also trying to exclude pulmonary embolism. The image quality was acceptable to diagnose or exclude aortic dissection, figure 5.52.

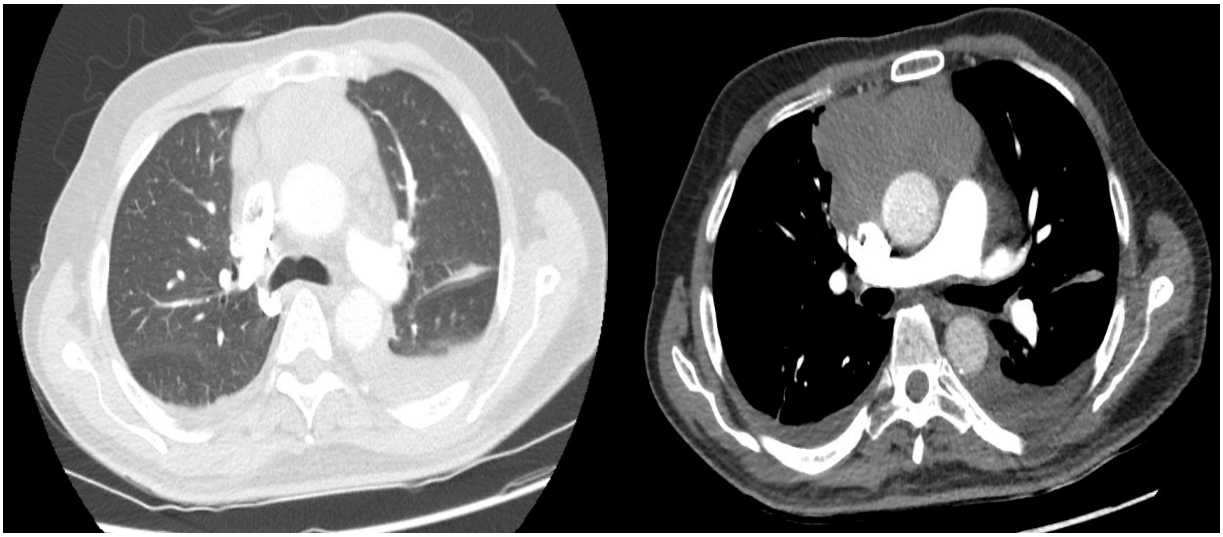
Furthermore, areas that can be investigated in the future are assessing focal lung disease entities, including lung nodules, masses, and consolidation and cavitary lesions.

This protocol can be used to follow up pulmonary nodules and solve lung parenchymal opacities that may appear in chest x-rays. The following case is an example of this. In the initial chest x-ray in figure 7.5, the radiologist detected a little pleural fluid at the left lung base and a linear scar at the left lung base, and a little consolidation at the left lung base. The lungs were otherwise reported clear. However, the patient had a persisting fever, tachycardia with oxygen requirement, and further low dose CTPA imaging revealed a large anterior mediastinal mass (Figure 7.6).



a b

Figure 7. 5: The heart is enlarged with a cardiothoracic ratio of 20/32 (a,b) There is a little pleural fluid at the left lung base and a linear scar at the left lung base. There is a little consolidation at the left lung base. The lungs are otherwise reported to appear clear.



a b

Figure 7. 6: Low dose CTPA shows large anterior mediastinal mass associated large pericardial and pleural effusion (a,b).

Differential considerations of the above mass include lymphoma, thymic neoplasm, germ cell tumour and metastatic.

7.4.12: The Original Contribution

The original contribution that emerged from this study is that a new low dose CT pulmonary angiogram has improved practice by reducing suboptimal exams and radiation dose to thousands of patients in the past 14 months. This protocol advanced pulmonary imaging. It is currently the primary imaging protocol for PE suspected patients. It continues to improve diagnosis while using radiation dose, which is significantly lower than the previous protocol.

Hence, this study recommends other imaging departments change their standard CT pulmonary angiogram protocol to this novel low dose CT protocol to reduce the risk of radiation exposure, especially to young patients. A larger cannula with a higher injection rate of 5ml/s should be utilised to increase the CT contrast enhancement. Patient education on breathing should be implemented with active coaching and relaxation techniques to achieve a gentle breath-hold with their mouth open to decrease Valsalva and potential motion artefact.

Patients under 105kg should be allocated to an enhanced low tube voltage of 80kV with altered reconstruction algorithm-kernel FC 51, a standard deviation setting of level 8 (Sure Exposure 3D), the image reconstruction process AID 3D strong, tube current modulation and an effective mAs of 258. The image quality of the low dose CTPA was diagnostically acceptable, and a significant radiation reduction was observed when a lower tube voltage with an adjusted SD level was utilised. This validates lower tube voltage with adjusted SD level as a useful technique for reducing radiation dose and suboptimal studies while maintaining excellent image quality for pulmonary embolism imaging.

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7.5: Conclusion

This research project has presented a new low dose CT pulmonary angiogram protocol, which significantly reduced radiation exposure and suboptimal examinations without affecting image or diagnostic quality. This study has used several methods to assess the CTPA protocol application, including retrospective review, prospective comparative studies, and questionnaires presented to radiologists and emergency medical doctors to achieve these goals.

This study has confirmed the acceptability of the protocol to both emergency medicine and radiology doctors. The new CTPA protocol image quality assessment has shown that it has acceptable imaging and diagnostic quality compared to that obtained with the 100kV standard protocol. It was also found that low dose CTPA produces predictable good image quality with no significant variation in diagnostic accuracy and image quality in comparison to the 100kV standard protocol. This study has demonstrated this protocol's robustness in the most common setting, in an emergency imaging department.

The study has established that the new low dose CTPA protocol results in significantly less radiation exposure compared to the 100kV standard protocol. The mean radiation dose of the low dose CTPA was decreased by 60% whilst using the improved 80kV protocol compared to the 100kV standard protocol. The average effective dose was significantly lower (1.005mSv) compared with the standard 100kV protocol (3.03mSv).

The study also found that contrast enhancement was considerably greater with the new protocol and markedly reduced suboptimal examinations. Contrast enhancement was increased by up to 60% whilst using the new low dose CTPA protocol. The contrast enhancement improvement significantly decreased suboptimal examinations in those patients undergoing the new low dose CTPA protocol. As my secondary goal, this study further reduced suboptimal scans by first reducing Valsalva with a gentle breath-hold with an open mouth technique rather than the standard breath-hold technique; this significantly reduced the rate of suboptimal scans. Secondly, testing the cannula with an 18 ml saline while the patient arm is in scanning position also reduced cannula failures, contrast extravasations and suboptimal examinations.

The other arm of the study has found multiple causes of CTPA overuse in the emergency medicine setting; the solution to this issue, like its cause, would be multifactorial. The major societal, legal and economic issues that cause overuse are beyond the remit of this thesis; however, imaging departments can scan patients with this new protocol with confidence that they

will be able to reduce the radiation dose to the patient whilst not missing PE or alternative diagnoses.

The study concludes that the new CTPA protocol using improved 80kV with gentle breath-hold with an open mouth could permit imaging departments to achieve excellent contrast enhancement, lower rates of suboptimal examinations and reduced patient radiation dose without affecting the image quality.

Appendices

Appendix I Differential Diagnosis

Differential Diagnosis of Pulmonary Embolism Questionnaire

Researcher:

My name is Ahmed Hashi, I am a PhD candidate at Australian National University Medical School, and my current study work focuses on CT pulmonary angiogram radiation optimisation.

Project Title:

Optimising Radiation dose of CT pulmonary Angiogram

Aim:

To identify the alternative or differential diagnoses on CTPA

Q1. Please rank the following in order of the 7 most common alternative or differential diagnosis to PE that causes pleuritic chest pain. 1 being the most common and so on:

Aortic Dissection
Pneumothorax
Pneumonia
Asthma on exacerbations
Atelectasis /collapse
Bronchiectasis
Rib fracture
Fibrosis
Chronic Obstructive Lung Disease – emphysema on exacerbations
Acute Coronary Syndrome
Pericarditis
Lung Cancer
Pulmonary Hypertension
Other alternative diagnoses…….

Q2. Please rank the following in order of the 7 most common alternative diagnosis to PE that causes dyspnea. 1 being the most common and so on:

Acute coronary syndrome
Congestive heart failure
Chronic obstructive pulmonary disease emphysema on exacerbations
Asthma on exacerbations
Pneumothorax
Atelectasis /collapse
Bronchiectasis
Rib fracture
Pneumonia
Influenza
Pericardial effusion
Panic attacks
Lung/Bronchi Cancer
Interstitial lung disease
Other common alternative diagnosis …….

Q3. At which level would you conduct a CTPA for a positive D-dimer?

- ☐ A > 0.5 1mg/L
- ☐ B > 0.7 1mg/L
- ☐ C >1 mg/L

Appendix II Image Quality

CTPA Image Quality Questionnaire

Researcher:

My name is Ahmed Hashi, and I am a PhD candidate at ANU College of Health and Medicine at the Australian National University.

Project Title:

Optimizing Radiation dose of CT pulmonary Angiogram

Q1. Image noise criteria have (4 levels):

1 = minimal image noise

2 = less than average noise

3 = average noise

4 = unacceptable image noise

Q2. Classic artefacts (4 levels):

1 = no artefacts

2 = negligible artefacts

3 = major artefacts, PE diagnosis still possible

4 = extensive artefacts making the image non-diagnostic image

Q3. Image quality (4 levels):

1 = unacceptable for diagnostic purposes

2 = somewhat suboptimal

3 = good

4 = excellent

Q4. Diagnostic overall confidence in detection of PE (4 levels):

1 = poor confidence

2 = confident only for limited clinical situation

3 = probably confident

4 = completely confident

Q5. Diagnostic overall confidence in detection for alternative lung diseases with the exception of interstitial lung diseases these include consolidation- pneumonia, masses, large nodules, extensive emphysemas and lung atelectasis (4 levels):

1 = poor confidence

2 = confident only for limited clinical situation

3 = probably confident

4 = completely confident

Q6. What is your preferred imaging modality of PE imaging

I.	Low dose CTPA	Yes ……	No ……..
II.	V/Q scan	Yes ……	No ……..

Appendix III CT Overuse Questionnaire

CT Pulmonary Angiogram Overuse Questionnaire.

Researcher:

My name is Ahmed Hashi, and I am a PhD candidate at ANU College of Health and Medicine at the Australian National University. My current study work focuses on CT pulmonary angiogram radiation issue.

Project Title:

Optimising Radiation dose of CT pulmonary Angiogram

With regards to CT pulmonary angiogram overuse:

Q1. Doctors are unaware of the risk of radiation dose
Strongly agree
Agree
Neither agree nor disagree
Disagree
Strongly disagree

Q2. Patients have not been informed about the risks of radiation.
Strongly agree
Agree
Neither agree nor disagree
Disagree
Strongly disagree

Q3. There is a lack of regulation in CT pulmonary angiogram use

Strongly agree
Agree
Neither agree nor disagree
Disagree
Strongly disagree

Q4. Health providers in emergency departments fear a lawsuit
Strongly agree
Agree
Neither agree nor disagree
Disagree
Strongly disagree

Q5. PE Symptoms are similar to other acute respiratory illnesses.
Strongly agree
Agree
Neither agree nor disagree
Disagree
Strongly disagree

Q6. The lack of experience in junior doctors can contribute to CT overuse
Strongly agree
Agree
Neither agree nor disagree
Disagree
Strongly disagree

Which other factors do you believe contribute to CT overuse?

How Can We Reduce CTPA Overuse?

Q1. Educating doctors about the risk of radiation can reduce the radiation dose.
Strongly agree
Agree
Neither agree nor disagree
Disagree
Strongly disagree

Q8. Educating patients about the risk of radiation can reduce the radiation dose.
Strongly agree
Agree
Neither agree nor disagree
Disagree
Strongly disagree

Q9. Use of D-dimer test/probability testing such as (Wells score, Geneva score) may reduce CTPA overuse
Strongly agree
Agree
Neither agree nor disagree
Disagree
Strongly disagree

Q10. Which other factors do you think could reduce radiation dose from CTPA

Appendix IV Participant Information Sheet

Participant Information Sheet

Researcher:

My name is Ahmed Hashi, and I am a PhD candidate at ANU College of Health and Medicine at the Australian National University.

Project Title:

Optimising Radiation dose of CT pulmonary Angiogram

General Outline of the Project:

I am undertaking this research project optimising the radiation dose of CT pulmonary Angiogram. The aim of this research is to reduce radiation dose and non-diagnostic exams in patients with suspected pulmonary embolism; this is to make sure that exposure is at its lowest level in the absence of damaging the image quality.

How much radiation dose will I get?

In this research project, you will get less radiation than a normal CTPA scan, between 0.4 to 1.8 mSv. The background radiation per year is about 3mSv.

What effect does the dose reduction will have on image quality?

Image quality may be effected only patients with large body habitus due to increased image noise, but the images will still be diagnostic.

The result (data) from this research:

The data from this research will be used to produce peer-reviewed published articles and conference and educational presentations.

However, as per The ANU Privacy Policy, any of the patient's demographic information (names, date of birth) will not be removed from the hospital system. We will maintain strict confidentiality to all information that is provided to us. The data will be kept in Calvary and ANU secure storage services with password protection.

Voluntary Participation & Withdrawal:

Participation in this research is voluntary to all patients, and you may decline to take part or to withdraw from the study at any time until the work is prepared for publication. If you withdraw, the data collected prior to withdrawal will be destroyed and not used for publication.

Name ……..

Signature .....

Date .....

Weight .....

Appendix V New Low Dose CT Pulmonary Angiogram Protocol

New low dose CT Pulmonary Angiogram

Pulmonary angiogram protocol for:

- patients weighing less than 105kg.

This study adheres to a limit of 80kV in patients weighing less than 105kg because a small trial of patients found that patients weighing more than 105kg required higher tube voltage (100kV)

- Pregnant patients less than weighing 113kg.

Patient preparation

Patient nil by mouth 4 hours prior to the examination time.

In some cases, when the PE is life-threatening, no special preparation is needed.

- The referring doctor or patient is required to complete a contrast information form and answer questions such as previous contrast reaction to contrast, asthma, diabetes, metformin, kidney disease, thyroid diseases, and pregnancy has to be checked.
- On-duty radiographers should always check the contrast information form, obtains creatinine and glomerular filtration rate to see how well the kidney is working if available.
- The patient should preferably have an 18-gauge cannula in the cubital fossa that flushes freely, this should be tested prior to the CTPA.

Patient position and contrast

- Patients should be in a supine position.
- Feet first
- Craniocaudal positioning
- Topogram centring point – Lung apices
- Instruct patient to take a small breath in and hold while opening the mouth
- Tomogram/ scan range: entire chest in a supine position.
- Contrast: Isovue 370
- Injection site: Right Cubital Fossa

- Contrast Volume: 50ml.
- Saline chaser: 50ml
- Contrast Flow Rate: 4-5ml/sec
- Bolus tracking on the pulmonary trunk.
- Monitoring – Pulmonary Trunk.
- Start delay – 5sec
- Pregnancy patients Bolus triggering with a short start delay time of 2- 3 seconds is required.

Starting location: Diaphragms
Ending location: Apices

Parameters

	kV	mAs eff	Rotation	Pitch	Detector Collimation
Low dose	**80**	**215**	**0.37s**	**0.8**	**0.5 x 80**

- Recontraction algorithms are FC17 for the mediastinal window, FC51 for the lung window.
- The standard deviation is level 8.
- The recontraction process is AID3D Strong.

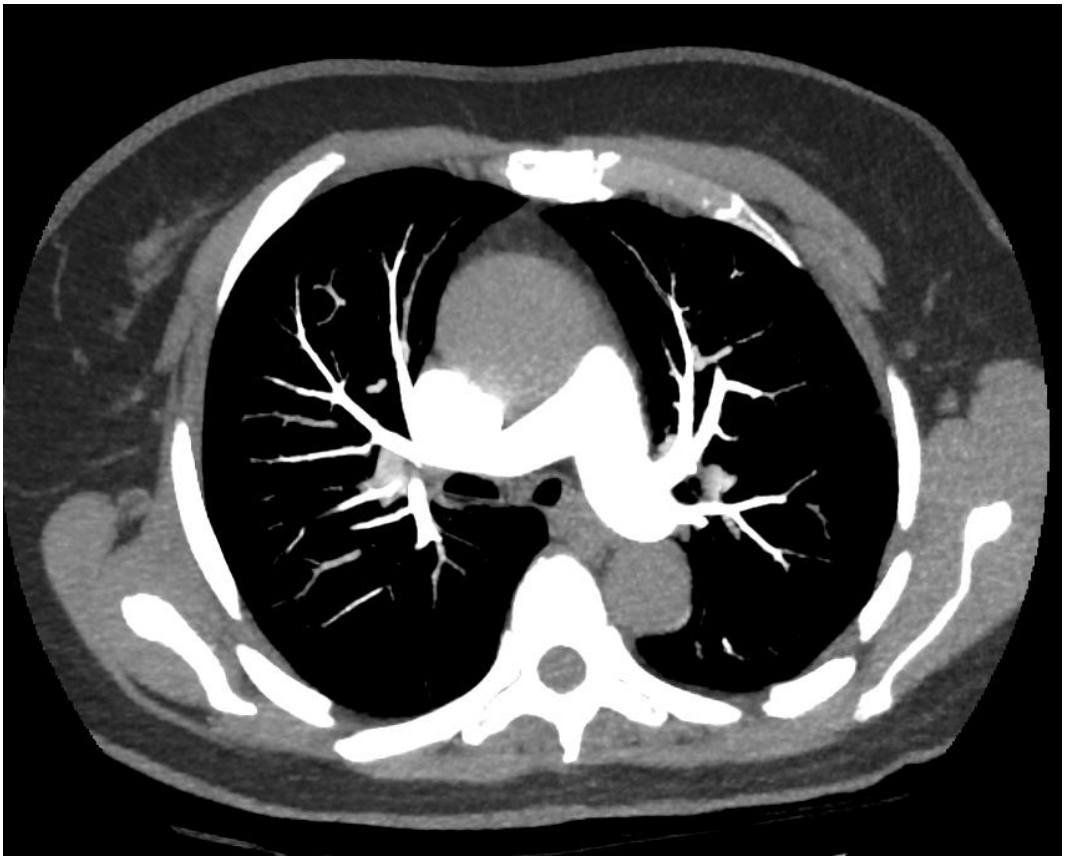

Figure 7. 7: Axial Mediastinum window of low dose CTPA.

Reconstructions

	RECON 1 Axial	RECON2 Axial		RECON 3 Axial	RECON 4 Axial
SLICE WIDTH	5mm	0.75mm		8mm	**1mm**
INTERVAL	5mm	0.5mm		8mm	**1mm**
KERNEL	B30f	B25f		B70f	**B30f**
WINDOW	**Mediastinum**	**Mediastinum**		**Lung**	**Mediastinum**

Overall, patient education, lower tube voltage, high injection, and excellent venous access enhances contrast enhancement within the subsegmental pulmonary arteries and decreases the possibility of suboptimal examinations

Award

Australian Capital Territory Health Directorate Award 2020.

I am so delighted to receive Australian Capital Territory Health Directorate, 2020 Research Excellence Award, for excellence in medical radiation research and contribute to ACT public radiology departments in developing a new low dose protocol for imaging pulmonary embolism and acute alternative respiratory diseases. This type of prize is awarded to health professionals each year with quantifiable achievement as set by ACT Health conditions. Helen Matthews, Chief allied health officer and professional leadership educator in the ACT Health Directorate, presented the award on 14 of October 2020.

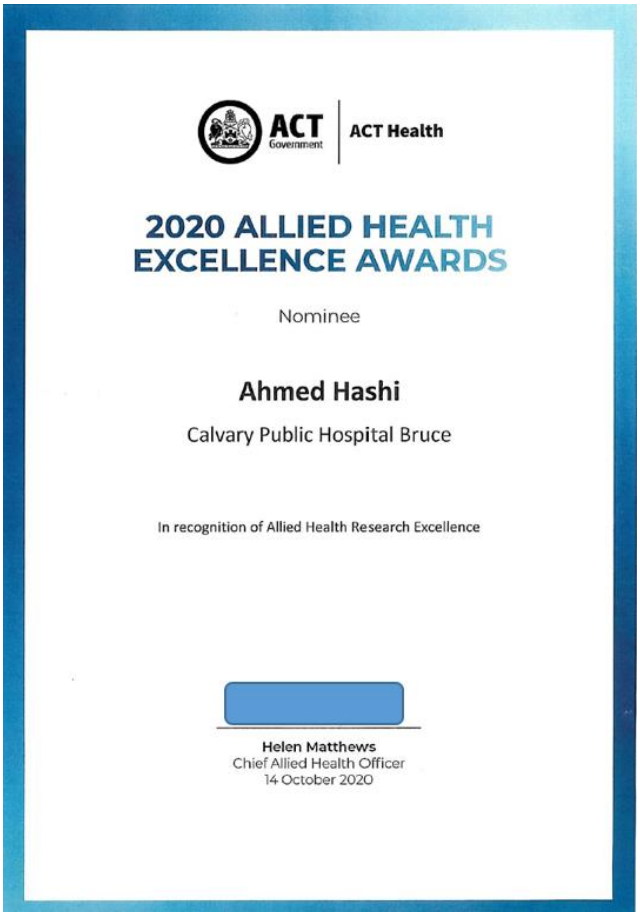

Figure 7. 8. ACT Government Health Directorate Allied Health Research Excellence Award 2020.

Publications

The following papers have been published or accepted for publications.

1) Approaches to Reduce the Rate of Suboptimal CT Pulmonary Angiograms
2) CT Pulmonary Angiogram with Reduced Radiation Exposure at Low Tube Kilovoltage
3) Optimised CT Pulmonary Angiogram Protocol in Pregnant Patients with Suspected Pulmonary Embolism.

Articles 1 and 3 have been accepted for publication, article 2 is awaiting publication.

Conferences and Presentations

I have presented the following presentations:

1) Cannon-Toshiba CT education day conference presentation at Canberra University' 2019, Topic: Ways to reduce radiation in CT pulmonary angiogram. A guide to dose minimisation in CT pulmonary angiogram. Role of low tube voltage in radiation reduction.
2) Calvary Hospital. Topic: Ways to decrease Valsalva manoeuvre and suboptimal in CT pulmonary angiogram. 2018.
3) Calvary Hospital. Topic: Ways to decrease suboptimal examinations in pregnant patients while using lower tube voltage, high injection and excellent venous access to improve contrast enhancement within the sub-segmental pulmonary arteries as well as decreases the possibility of suboptimal examinations, 2019.
4) Australian National University Medical School 1st HDR Symposium 2019, topic 'diagnostic accuracy in low tube voltage CT pulmonary angiogram and factors affecting radiation dose in CTPA.
5) Australian National University Medical School 2nd HDR Symposium 2020, differential diagnosis of pulmonary embolism and approaches to reduce the rate of suboptimal CT pulmonary angiograms.

I would like a knowledge that the planned International conference in 2020 has been delayed due to impact of COVID 19.

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