A RETROSPECTIVE REVIEW OF COMPUTED TOMOGRAPHY PULMONARY ANGIOGRAPHY IMAGE QUALITY AND THE IMPACT ON DIAGNOSTIC OUTCOME AT A TERTIARY SOUTH AFRICAN HOSPITAL

by

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ABSTRACT

Background:

Computed Tomography Pulmonary Angiography (CTPA) is a key diagnostic imaging modality for pulmonary embolism. These studies are technically challenging to perform. Degraded image quality may result from inadequate pulmonary artery contrast opacification, motion- or streak artefact as well as patient factors. Literature suggests that poor quality scans could lead to indeterminate outcomes and suboptimal clinical decisions with risk of increased mortality.

Objective:

The study aimed to benchmark the image quality and diagnostic outcomes of CTPA studies in the setting of a tertiary Southern African hospital. The relationships between CTPA image quality and diagnostic and clinical outcomes, as well as related variables such as health risk factors and effective dose, were also explored.

Methods:

A retrospective cross-sectional study evaluated consecutive CTPA studies performed at Groote Schuur hospital, Cape Town, South Africa, over a six-month period from 1 July 2018 to 31 December 2018. All studies performed for suspected acute or chronic pulmonary embolism (PE) in patients 18 years and older were included. Records were reviewed regarding image quality and diagnostic and clinical outcomes. Correlation tests were performed between continuous variables and chi-square tests among categorical variables.

Results:

During the study period, 231 CTPA studies were performed, of which 226 were included. The sample comprised 69 % females and 31 % males, with median age of 45 years (range 19-84 years). In 204 (90.3 %) of studies, adequate contrast opacification ≥ 211 HU was obtained. Inadequate contrast opacification was present in 9.7% of cases, in line with previous research. Motion and/ or streak artefacts were present in 45.6%. PE was confirmed in 22% and excluded in 65 % of cases. The number of scans with indeterminate diagnostic results only comprised 30 out of the 226 scans reviewed, however, the percentage was higher than previously reported

(13.3% vs mean of 6.4 % in published literature). Amongst these, inadequate contrast opacification occurred in 15 (50 %) of studies and artefacts degraded image quality in 24 (80 %). Patients with a diagnosis of PE had higher mortality, compared to patients with negative and indeterminate scans. Clinicians interpreted indeterminate scans as negative, however, this did not impact adversely on mortality.

Conclusions

It was encouraging that the percentage of studies with adequate contrast opacification met published bench-marks. Although the higher-than-expected percentage of indeterminate studies may partially be explained by the prevalence of artefacts, it requires further investigation. This did not, however, translate into adverse mortality outcomes.

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ABBREVIATIONS

BP – Blood Pressure
CTA - Computed Tomography Angiography
CTPA – Computed Tomography Pulmonary Angiography
DLP – Dose-length product
DVT – Deep Venous Thrombosis
ED – Effective Dose
ESR – European Society of Radiology
EU – European Union
HIV – Human Immunodeficiency Virus
HREC – Human Research and Ethics Committee
HU – Hounsfield Units
kVp – kilovoltage peak
mAs – milliampere-second
MPOT – Main Pulmonary Outflow Tract
MR – Magnetic Resonance
mSv – milli-Sievert
PACS – Picture Archiving and Communication System
PE – Pulmonary embolism
PIOPED - Prospective Investigation of Pulmonary Embolism Diagnosis
PTE – Pulmonary thrombo-embolism
QA - Quality Assurance
QC – Quality Control
ROI – Region of Interest
RIS – Radiology Information System
SARS-2-COV - Severe acute respiratory syndrome coronavirus 2
SD – Standard Deviation
UCT – University of Cape Town
UK – United Kingdom
US – United States
VTE – Venous Thromboembolism
V/Q – Ventilation Perfusion

1. INTRODUCTION AND LITERATURE REVIEW

1.1. Background to the role of imaging in pulmonary embolism

1.1.1. Pulmonary embolism – why is it important?

Venous thromboembolism (VTE), encompassing deep vein thrombosis (DVT) and pulmonary embolism (PE), is a common clinical entity that carries a high morbidity and mortality. Globally it is the third most common cardiovascular cause of death, after coronary artery disease and stroke (Henzler *et al.*, 2011:13), (Danwang *et al.*, 2017:1770), (Bělohlávek, Dytrych and Linhart, 2013:3), (Konstantinides *et al.*, 2020).

Epidemiology

The exact epidemiology of pulmonary embolism is hard to determine due to its heterogenous presentation, ranging from incidental asymptomatic small vessel disease to rapidly fatal massive pulmonary embolism. Quoted incidence and fatality rates vary between publications, but it is agreed that pulmonary embolism is a major cause of mortality, morbidity, and hospitalisation.

Incidence and prevalence of VTE

European epidemiological models estimated over 370 000 deaths related to venous thromboembolism during 2004, in six countries of the European Union with a total population of 310 million. Extrapolated data from the six modelled countries estimated 1.1 million venous thromboembolic events, with 543,454 VTE related deaths across the whole EU (Cohen, Agnelli and Arcelus, 2007)(Wendelboe and Raskob, 2016).

European guidelines for the diagnosis and management of pulmonary embolism reported annual incidence rates of venous thrombosis and pulmonary embolism of approximately 0.5 to 1.0 per 1000 inhabitants. Actual figures are probably higher due to silent PE that can develop in up to 40% to 50% of patients with deep vein thrombosis (Bělohlávek, Dytrych and Linhart, 2013:129).

In the United states, a 25-year population based study estimated the overall incidence of VTE at 117 per 100 000 - just more than 1 per 1000 (Silverstein *et al.*, 1998). The authors concluded that VTE is a major health problem, especially among the elderly and hospitalised patients. According to Beckman et al (2010), VTE affects

300 000 to 600 000 people in the US annually, with significant mortality ranging from 10 to 30 % within 30 days.

Robust data on the prevalence of thromboembolic disease in Africa is limited.
A systematic review conducted from Cape Town during 2017 found wide variation in prevalence, with post-surgical, pregnant and postpartum patients particularly at risk. The authors highlight a higher mortality rate for PE among African patients, compared to figures published for Western countries, and noted that a quarter of patients at risk of venous thromboembolism were not receiving prophylaxis (Danwang *et al.*, 2017: 1770).

Another South African study found a pulmonary embolism prevalence of 26 % in a selected patient group who underwent CTPA angiography, with a statistically significant positive association between pulmonary embolism and tuberculosis, but not HIV (Ramlakhan, Andronikou and Rajkumar, 2017). A prior Cameroon university hospital based study found an incidence of 32.4 % of pulmonary embolism in patients who underwent CTPA based on high clinical suspicion (Tambe *et al.*, 2012).
A Cape Town autopsy series conducted during 2001-2005 identified pulmonary embolism as the third most common cause of natural death in females (Tiemensma and Burger, 2012). Large well designed epidemiological studies are, however, needed to determine the true prevalence of venous thromboembolism and pulmonary embolism in Africa (Danwang *et al.*, 2017:1779).

At the time of writing this thesis, the SARS-COV-2 coronavirus continued to spread in across the world and in Africa. COVID-19 disease is associated with coagulopathy and thrombotic complications, adding further to the burden of VTE. Optimal diagnostic and prophylactic strategies are therefore urgently needed in view of this increased risk for VTE in hospitalised patients with COVID-19 (Middeldorp *et al.*, 2020).

Clinical aspects and risk stratification

Early and accurate diagnosis of pulmonary embolism is crucial, as the overall mortality rate in untreated patients with acute pulmonary embolism is 30 %, increasing to 65 % in haemodynamically unstable patients requiring resuscitation.

Up to 10% of acute pulmonary embolism patients die suddenly. The majority of deaths occur within the first hour or two, due to complications such as right heart failure, hypotension, shock and cardiac arrest. Management is aimed at thrombolysis, reversing right heart failure and preventing re-occurrence (Bělohlávek, Dytrych and Linhart, 2013). Clinical risk stratification is used to determine appropriate management, based on definitions of haemodynamic instability denoting acute high-risk pulmonary embolism, as demonstrated in Table 1-1 below.

Table 1-1: Risk stratification as published in 2019 European Society of Cardiology Guidelines on the diagnosis and management of acute pulmonary embolism (Konstantinides *et al.*, 2020)**.**

Cardiac arrest	Obstructive shock	Persistent hypotension
Need for cardiopulmonary resuscitation	Systolic BP < 90 mmHg or requiring vasopressors to achieve adequate BP >90 mmHg	Systolic BP < 90 mm Hg or systolic BP drop ≥40 mmHg, lasting longer than 15 min and not caused by new-onset arrhythmia, hypovolaemia, or sepsis.
	AND	
	End-organ hypoperfusion and features of shock	

1.1.2. Role of diagnostic imaging in pulmonary embolism – CTPA to the rescue!

Challenges in diagnosing venous thrombosis and pulmonary embolism

It is clear that rapid and accurate diagnosis, combined with appropriate clinical risk stratification and prompt initiation of therapy, is needed to optimise management of life threatening acute pulmonary embolism. Detection of asymptomatic thrombo-embolic disease and ensuring appropriate prophylactic therapy should also be prioritised, as recurrence of embolism is a leading cause of death (Yazdani *et al.*, 2015: 1245).

However, the diagnosis of pulmonary embolism remains challenging although it is a common condition. Risk factors for VTE are multiple and non-specific, including cardiovascular disease, trauma, surgery, immobilisation, intensive care admission, pregnancy, obstetric and gynaecological factors, malignancy and infections (Bělohlávek, Dytrych and Linhart, 2013).

The clinical presentation tends to be vague with a wide differential diagnosis, including symptoms such as dyspnoea, chest pain, syncope and haemoptysis.
Individual clinical signs and symptoms, as well as chest radiograph and electrocardiogram findings, lack sensitivity and specificity. In contrast, combined findings, evaluated either by clinical judgement or prediction rules based on validated scoring systems, allow classification of patients with suspected pulmonary embolism into distinct categories of pre-test probability corresponding to prevalence (Konstantinides *et al.*, 2020). The post-test diagnostic outcome of imaging studies performed for the diagnosis of pulmonary thromboembolism, such as computed tomography (CT), is not only dependant on characteristics of the diagnostic test itself, but also determined by the clinical pre-test probability (Konstantinides *et al.*, 2020). The diagnosis of pulmonary embolism is therefore ideally based on a combination of clinical pre-test probability, D-Dimer level and imaging findings (Noschang *et al.*, 2018: 178-179).

Evaluation for pulmonary thromboembolism should start by determining the clinical pre-test probability using validated scores, such as the well-known Wells and Geneva scoring systems demonstrated below in Table 1-2 and Table 1-3, before deciding on appropriate imaging modalities.

Table 1-2: Geneva Clinical Prediction Score for pulmonary embolism (Noschang *et al.*, 2018)**.**

Criteria	**Score**
Risk factors:	
Age above 65 years	1
History of pulmonary thromboembolism	3
History of recent surgery or fracture within 1 month	2
Active malignancy	2
Symptoms:	
Unilateral arm pain	3
Haemoptysis	2
Signs	
Heart rate of 75 to 94 beats per minute	3
Heart rate > 94 beats per minute	5
Pain on palpation of arm veins, or oedema	4
Score	**Risk**
0-3	Low
4-10	Moderate
≥11	High

Table 1-3: Wells Score for pulmonary embolism risk stratification - Main risk factors for PTE – Wells Score (Noschang *et al.*, 2018:179).

Criteria		**Score**
Suspected venous thromboembolism		3
Alternative diagnosis less likely than PTE		3
Heart rate > 100 beats per minute		1.5
Immobilisation or surgery in the last four weeks		1.5
History of previous VTE or PE		1.5
Haemoptysis		1
Malignancy		1
Score	**Probability of PTE**	**Risk**
0-2	3.6 %	Low
3-6	20.5%	Moderate
>6	66.7 %	High

Brief overview of diagnostic imaging modalities for VTE.

Major advances in the diagnostic imaging of pulmonary embolism have been achieved during the last century, as outlined in a 2015 review paper produced by the Radiological Society of North America (Yazdani *et al.*, 2015).

Relevant modalities include chest radiography, ventilation perfusion (V/Q) imaging, lower extremity ultrasound, CT pulmonary angiography (CTPA), conventional catheter angiography and lately magnetic resonance (MR) imaging. Each of these modalities have advantages and limitations and choice should be determined by clinical considerations, guidelines, availability, technical and radiation dose considerations as well as patient specific factors.

Chest radiography

Chest radiographs are insufficient to confirm or exclude a diagnosis of pulmonary embolism. Findings are often non-specific, especially in cases without infarction. Better known signs include the Westermark sign of oligaemia (demonstrated in Figure 1-1 below), and the Hampton hump - a peripheral wedge-shaped opacity indicative of pulmonary infarction (Moore *et al.*, 2018: 226). Atelectasis, small pleural effusions and right ventricular failure are common but non-specific findings in the presence of pulmonary embolism. A chest radiograph should, however, always be performed whenever pulmonary embolism is suspected in order to diagnose other entities with a similar clinical presentation, such as pneumonia or pneumothorax, and to potentially aid in the interpretation of V/Q scans (Yazdani *et al.*, 2015:1246-1247).

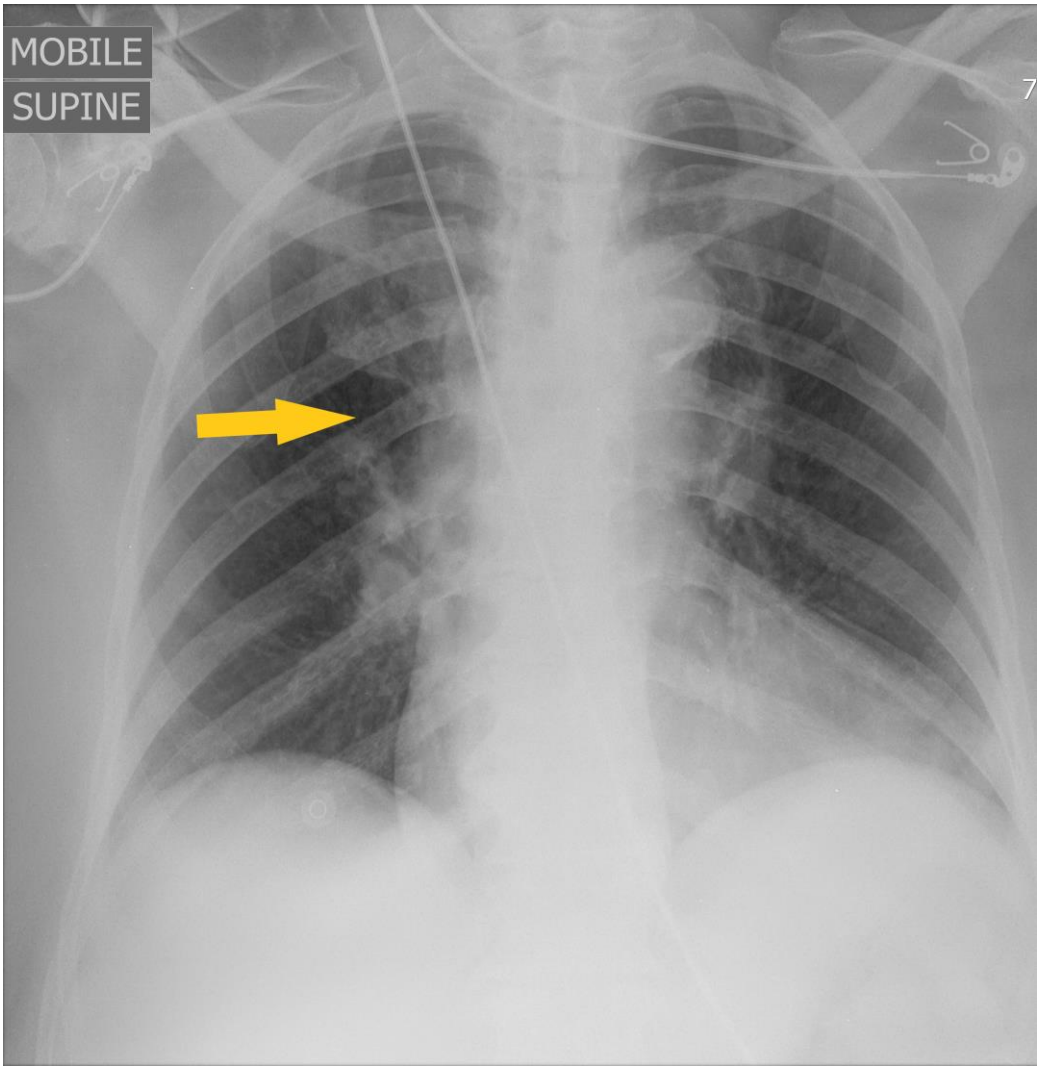

Figure 1-1: Chest radiograph demonstrating Westermark sign of oligaemia.

V/Q imaging

For 30 years, until the advent of newer computed tomography (CT) techniques, lung scintigraphy utilising radioisotopes for ventilation, perfusion, or both was the diagnostic study of choice for pulmonary embolism (Moore *et al.*, 2018:227). V/Q scans are interpreted along with a correlative chest radiograph performed within 12–24 hours. A peripheral wedge-shaped perfusion defect in a lobar, segmental, or sub-segmental distribution without a corresponding ventilation defect (i.e., a mismatched defect) is suggestive of pulmonary embolism. Modified PIOPED II criteria is applied to classify studies as high probability, very low probability, normal, and non-diagnostic (Moore *et al.*, 2018:227).

Although CTPA is the current gold standard, there are still clinical situations in which V/Q scan may be preferred, particularly renal failure, contrast material allergies, young females, and patients who cannot fit into the CT scanner. V/Q scan has a 50-fold lower radiation organ dose to the female breast (0.28–0.9 mSv versus 50–80 mSv in 64 slice CT) (Moore *et al.*, 2018:227). Due to this consideration, V/Q scanning is the preferred modality to rule out PE in pregnancy, provided the chest radiograph is clear (Cogley *et al.*, 2012:16).

Lower extremity ultrasound

The relationship between lower limb venous thrombosis and pulmonary embolism is well established. Pulmonary embolism commonly originates from a lower limb DVT, and rarely from upper limb thrombosis, usually after venous catheterisation (Konstantinides *et al.*, 2020). Real time B-mode ultrasound is the preferred modality for diagnosing deep venous thrombosis, although it requires a skilled operator and can be difficult due to patient factors such as morbid obesity, very tender lower limbs or variant venous anatomy (Yazdani *et al.*, 2015:1249-1250).

The role of ultrasound in the diagnosis of pulmonary embolism is mainly limited to patients who have localising lower limb symptoms suggestive of venous thrombosis. It may also be used as an adjunctive test for further work-up of patients with a low pre-test probability of pulmonary embolism and non-diagnostic lung scan results (Yazdani *et al.*, 2015: 1249-1251). Compression ultrasound may also be useful in diagnostic workup of patients with suspected VTE and contra-indications to CT (Konstantinides *et al.*, 2020).

Magnetic resonance angiography

The use of magnetic resonance angiography in the investigation of suspected pulmonary embolism is currently being evaluated in research settings. It has, however, not yet been implemented in widespread clinical use, due to low sensitivity and frequent indeterminate results (Yazdani *et al.*, 2015: 1255-1257). Availability in emergency settings is thought to be another limitation.

Conventional catheter angiography

Pulmonary angiography has largely been replaced by less invasive CT angiography as the preferred modality for the diagnosis or exclusion of pulmonary embolism. Diagnosis is based on evidence of thrombus, as filling defects or truncation of pulmonary arterial branches, on at least two projections. However, the procedure carries a 0.5% mortality risk, with major complications in 1 % and minor complications in 5%. Pulmonary angiography, especially digital subtraction angiography, is nowadays mainly indicated for catheter directed interventional treatment of pulmonary embolism (Konstantinides *et al.*, 2020).

Computed tomography pulmonary angiography (CTPA)

The Second Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED II) trial was the first large prospective, multicentre study of the accuracy of multidetector CT angiography in the diagnosis of acute pulmonary embolism. It demonstrated 83 % sensitivity and 96 % specificity of CT angiography in patients with a known reference diagnosis, excluding inconclusive studies (Stein *et al.*, 2006). Positive predictive values were dependent on clinical concordance, with a high value of 96% in cases where the clinical assessment was in agreement with the outcome of the CT findings, 92 % with intermediate clinical correlation and non-diagnostic outcomes when clinical probability was discordant (Stein *et al.*, 2006). Accuracy was found to be further increased when CTPA was combined with CT venography techniques to assess for the presence of deep vein thrombosis.

The PIOPED II study was conducted with mainly 4 slice and a few 16 slice scanners, so it likely underestimates the accuracy of newer 64 slice and dual source CT scanners. Technological advances in the development of multidetector CT scanners with excellent spatial and temporal resolution now allows for rapid acquisition of CTPA imaging of with substantially improved image quality (Henzler *et al.*, 2011). CT angiography has conveniently become available around the clock in all major centres worldwide.

An advantage of CTPA is that it not only accurately demonstrates occlusion or filling defects in the pulmonary arterial bed, but can also simultaneously evaluate associated pathology such as lung infarction. In the case of positive scans confirming pulmonary embolism, risk stratification can be performed, for example by using accepted arterial obstruction scores such as the Qanadli score (Qanadli *et al.*, 2001) and by CTA assessment of right ventricle dilation (Bělohlávek, Dytrych and Linhart, 2013: 135).

Visualisation of the entire thorax allows for diagnosis of diseases of the lung parenchyma, mediastinum, pleural or pericardial spaces and thoracic aorta. Life-threatening causes of chest pain and dyspnoea such as aortic dissection can be ruled out simultaneously (Bělohlávek, Dytrych and Linhart, 2013: 135). It is therefore not surprising that CTPA has become the imaging modality of choice for investigation of acute pulmonary embolism, and features prominently in many diagnostic algorithms, with a resultant explosive growth in the number of studies requested over recent years.

Concerns have, however, been raised regarding increasing population radiation exposure in medical imaging, and potential for renal and allergic adverse reactions related to use of radiographic contrast media (Rowe *et al.*, 2017: 654). It therefore remains important that clinicians adhere to validated guidelines and clinical scoring systems to ensure appropriate requests.

Figure 1-2 and Figure 1-3 show how good quality CTPA images can aid the diagnosis of pulmonary embolism. Filling defects in the contrast filled pulmonary arterial system are clearly demonstrated.

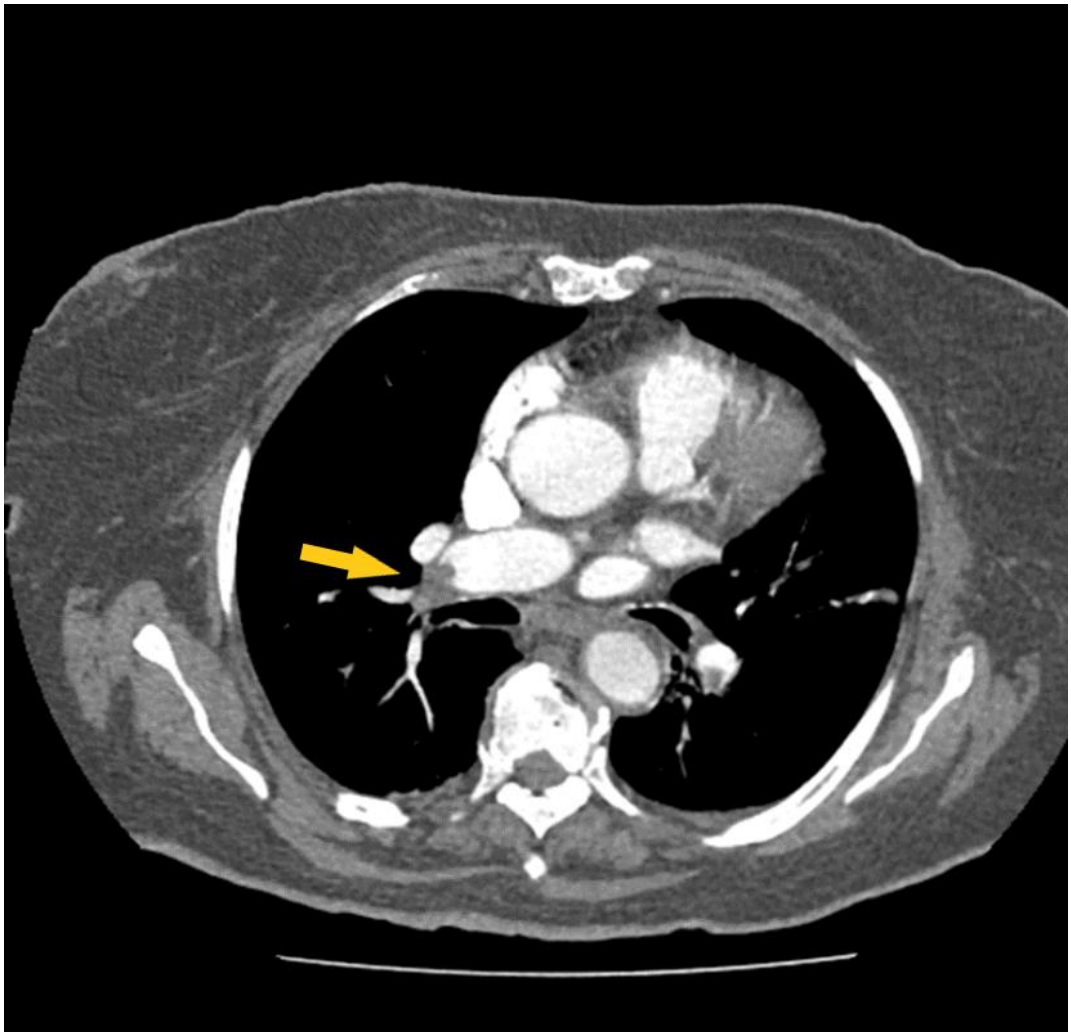

Figure 1-2: CT Pulmonary angiogram demonstrating filling defects in the lower lobar arteries bilaterally indicative of pulmonary embolism.

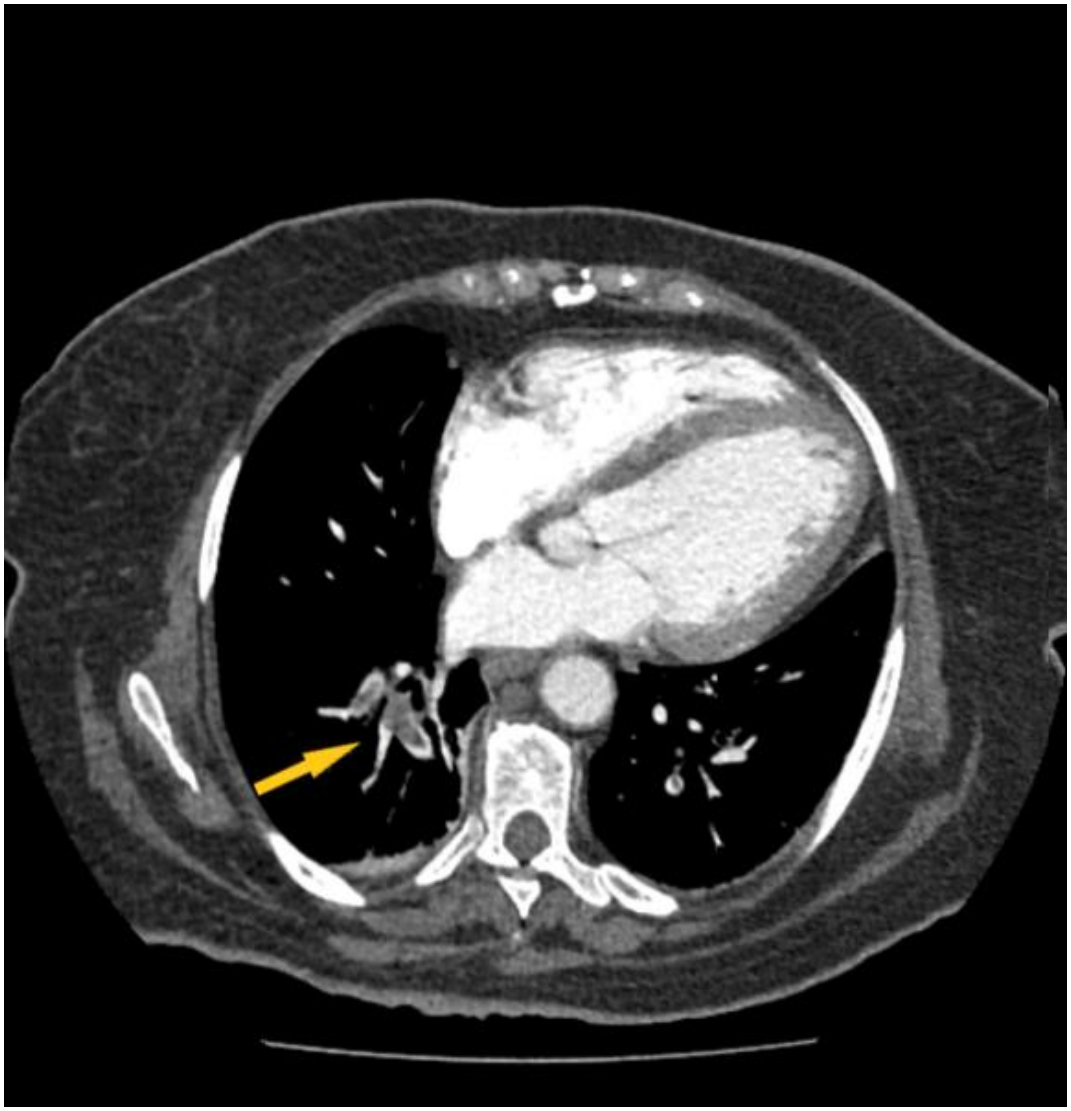

Figure 1-3: CT Pulmonary angiogram demonstrating filling defects in right lower lobe segmental pulmonary arteries.

In Figure 1-4 a coronal CTPA slice on lung window settings shows a wedge-shaped right lower lobe lung infarct associated with pulmonary embolism.

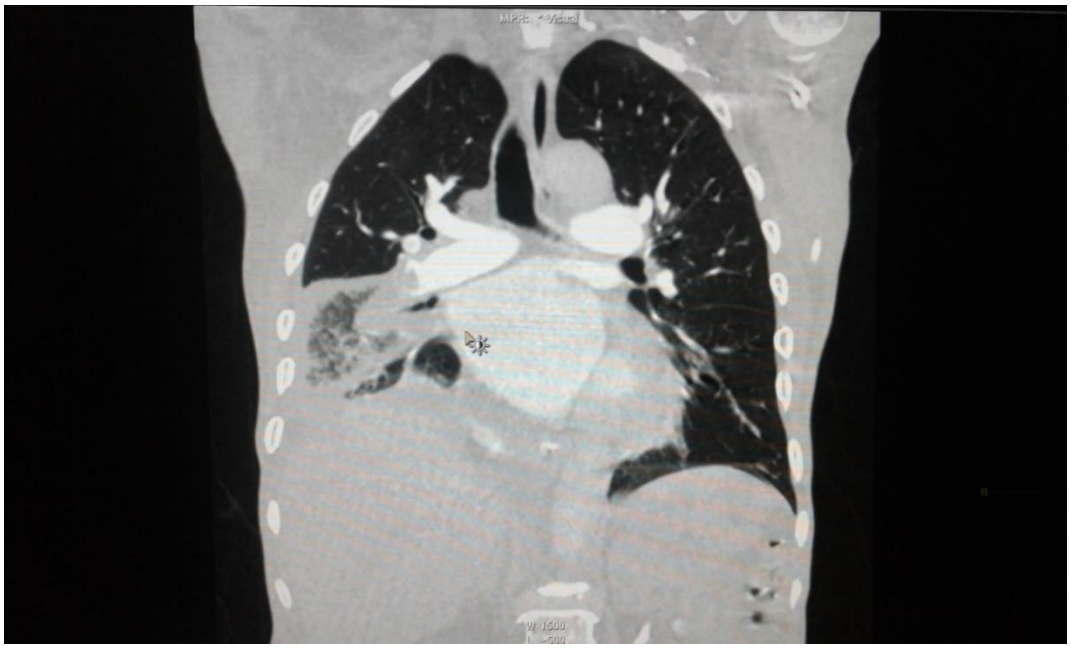

Figure 1-4: CT Pulmonary angiogram on lung window setting – wedge shaped right sided lung infarct associated with pulmonary embolism.

1.1.3. The dilemma of the indeterminate CTPA

The advent of modern CT angiography techniques has revolutionised the diagnosis of acute pulmonary embolism. However, in a small percentage of studies the image quality is too poor to allow a firm diagnosis, despite evolving multidetector scanner technology. The mean rate of 'non-diagnostic' or 'indeterminate' studies is quoted as 6.4% (0.5 – 10.8%) in the literature, with poor contrast opacification and motion artefact given as the main degrading factors (Yeo, Zhou and Lim, 2017: 18-19), (Jones and Wittram, 2005:329).

This is important because clinical management of suspected pulmonary embolism is directly guided by imaging. Low pre-test probability has been linked to indeterminate outcomes, which is concerning as inconclusive studies influence clinical decision making and patient care. Positive investigations often lead to anticoagulative therapy or placement of a vena cava filter. Negative studies may provide an alternate diagnosis. Indeterminate studies are often incorrectly regarded as 'negative' with a

risk that pathology may be missed and no further appropriate action is taken (Jones and Wittram, 2005:366). In a recent study (Yeo, Zhou and Lim, 2017: 22-23), 33 % of the suboptimal studies were regarded as negative endpoints by the clinicians.

1.1.4. Radiologist reporting and interpretation of CTPA

Research by Sabel et al (2017) concluded that referring clinicians and pulmonologists preferred structured CTPA reports to conventional prose style reports, rating it higher in content and clarity. However, patient management was not affected by the style of reporting (Sabel *et al.*, 2017:191).

A large retrospective study reviewing 840 consecutive CTPA studies, showed that radiology residents provided high level interpretation of CTPA studies conducted after hours. Good concordance (90%) was found between the resident interpretation and subsequent consultant radiologist overview. It was, however, commented that excellent image quality resulted in better interobserver agreement (Cervini *et al.*, 2008). Regardless of the reporting style or level of experience of the interpreting radiologist, a good quality scan is likely to render a conclusive diagnosis.

1.2. Introduction to technical aspects influencing CTPA image quality and diagnostic yield

1.2.1. Pulmonary artery contrast opacification

Minimum required attenuation of blood when imaging pulmonary emboli

In computed tomography, iodated intravascular contrast material is used to increase the radiographic attenuation of intravascular blood, thereby rendering vessels visible upon imaging. For clots and any intraluminal non-opacified filling defects to be visible, there must be an adequate difference in attenuation between opacified blood and the clot. In a seminal paper on CTPA technique, (Wittram, 2007), the theoretic minimum attenuation of blood that is required to detect all acute and chronic pulmonary venous thrombi is given as 93 and 211 Hounsfield Units (HU) respectively. Other researchers have subsequently used 211 HU as cut-off value for adequate pulmonary arterial contrast enhancement (Muenzel *et al.*, 2017: 131) or 250 HU as optimal value (Yeo, Zhou and Lim, 2017: 18-19).

Factors influencing pulmonary arterial contrast enhancement

Adequate pulmonary arterial contrast enhancement is dependent on multiple interrelated factors including contrast administration, scan timing and other technical parameters, as well as intrinsic patient factors: Factors related to contrast administration include adequate site and calibre of intravenous access route as well as rate of contrast injection, which is dependent on cannula size. Ideally, contrast should be administered via an 18 to 20 g cannula in the antecubital fossa. A power injector and saline chaser bolus is commonly used. Dual energy scanning, when available, could be considered in patients where venous access is restricted to small peripheral veins. Contrast dose varies depending on patient size and institutional protocol. Contrast extravasation during the scan or flow mixing artefact are factors that can degrade image quality. High risk patients include the infants, elderly, uncooperative or unconscious patients. An alternative intravenous access site should be obtained and the scan could be repeated in the arm down position.

Correct scan timing is important, using either a test bolus or bolus tracking methods, and correct placement of a region of an interest (ROI) in the main pulmonary artery.
Other technical considerations include kVp and mAs settings, with effects both on image quality and radiation dose. CTPA can be performed as inspiratory, free breathing or expiratory imaging, with better contrast opacification during free breathing or expiratory imaging. Lastly post processing software algorithms are utilised to retrospectively enhance image quality (Muenzel *et al.*, 2017: 131).

Intrinsic patient related factors include body habitus, venous anatomy and pregnancy, cardiac dysfunction, respiratory failure, congenital variants or thoracic venous outlet obstruction (Chaturvedi, Oppenheimer and Raijah *et al.*, 2017:128). Renal or immunological factors may limit contrast administration or dose (Wittram, 2007).

Flow artefact resulting in inadequate contrast enhancement

Increased inflow from the vena cava to the right atrium may result in mixing of non-opacified blood with injected contrast from the upper extremity, causing inadequate contrast opacification within the pulmonary arteries.

The resultant flow artefact and pseudo-filling defects may render the CTPA study non-diagnostic, and repeat imaging may be needed if thrombus is suspected.

Decreased opacification of multiple bilateral pulmonary arteries at the same level without vessel lumen distention may alert the reader to the presence of this artefact (Chaturvedi, Oppenheimer and Raijah *et al.*, 2017:135). As this inflow is a normal response to negative intrathoracic pressure, the problem is exaggerated by the practice of hyperventilation prior to scanning. (Somanathan and Saade, 2012: 4). A favourable outcome has been shown by repeating nondiagnostic CTPA in expiratory phase, improving pulmonary arterial enhancement through eliminating this transient mixed attenuation artefact (Chen Y H *et al.*, Velayudhan, Weltman, D I. 2008: 161).

Examples of CTPA images demonstrating adequate and suboptimal pulmonary artery contrast opacification.

Figure 1-5 is an example of a good quality CTPA study with adequate contrast opacification of the main pulmonary artery. Bright white high attenuation contrast is present in the MPOT. Compared to that the relatively low density in the aorta appears greyish.

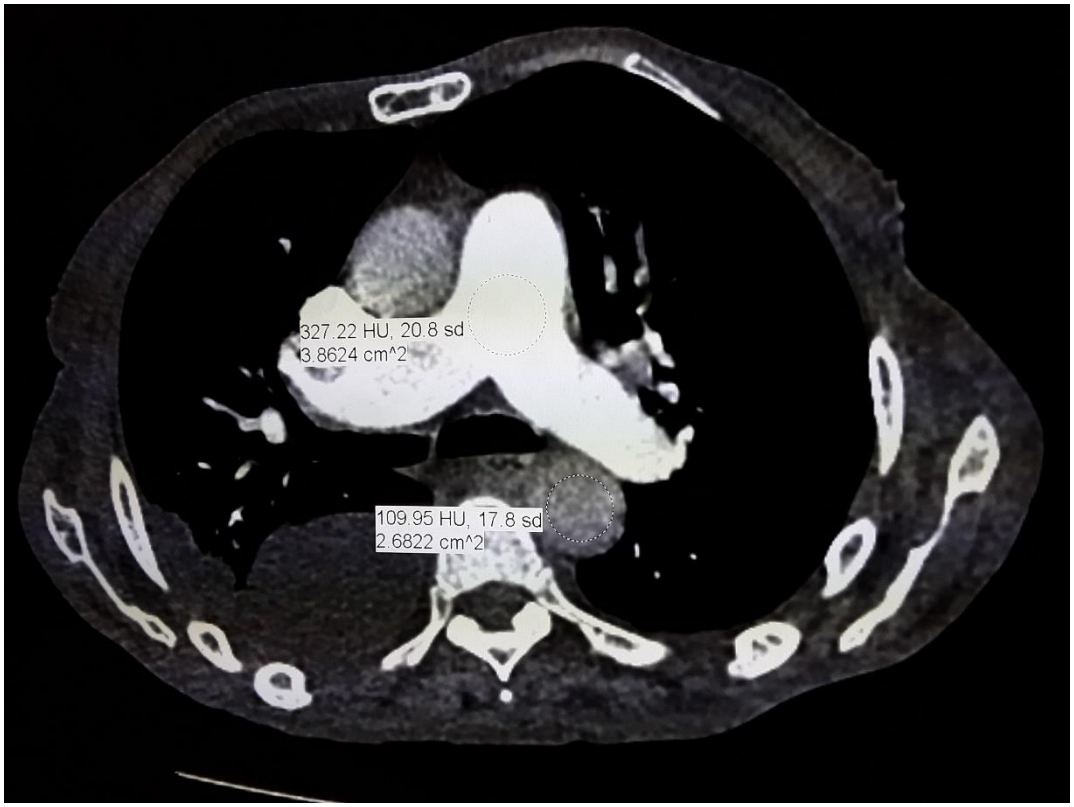

Figure 1-5: Good quality CTPA image with adequate contrast opacification of the main pulmonary artery (327 HU), compared to relative low density in the aorta.

Figure 1-6 below demonstrates a poor quality CTPA study with inadequate contrast opacification in the main pulmonary artery measuring only 140 HU, which is below the required minimum of 211 HU and also lower than the density in the aorta.

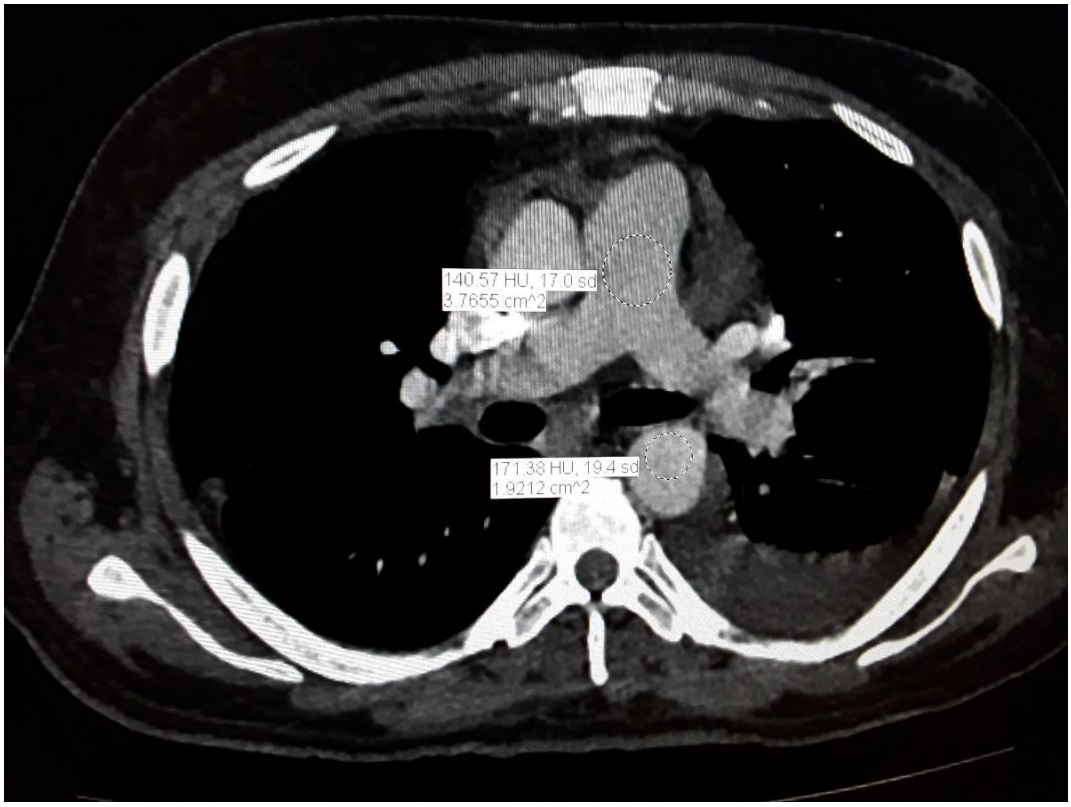

Figure 1-6: Example of indeterminate CPTA study due to inadequate contrast opacification in the main pulmonary artery (140 HU) compared with the aorta (171 HU), likely due to incorrect scan timing.

1.2.2. Seagulls, streaks and stripes – common artefacts known to degrade CTPA image quality

Radiographers and radiologists should be aware of artefacts that can lead to incorrect interpretation or indeterminate outcome of CTPA studies (Somanathan and Saade, 2012: 2). Physics, patient factors, pathology and scanner parameters should all be taken into account to plan in advance for optimal image quality and outcome.

Motion artefact.

Along with inadequate contrast enhancement, respiratory motion artefact is a major cause for indeterminate CTPA scan outcomes (Wittram, 2007: 1256). This problem

is frequently encountered as CTPA imaging tend to be requested in dyspnoeic patients. Although advanced multidetector scanners only require a 10 second breath hold, CTPA is still difficult to perform in patients who are short of breath. Due to the rapid positional change of pulmonary vessels, a characteristic seagull wing appearance is seen on lung window settings (Yeo, Zhou and Lim, 2017:22).

In addition, partial volume averaging of lung parenchyma and vessels may cause apparent filling defects. Aortic root and cardiac motion artefact may be problematic in patients with hyperdynamic circulation (Lau, Jackson and Kuganesan, 2015:6).

The incidence of motion artefact has, however, decreased with advances in multidetector CT scanner capabilities with faster image acquisition at higher spatial resolution (Chen *et al.*, 2008).

Streak/ beam hardening artefact

Streak artefact commonly occurs due to dense contrast in the superior vena cava, or presence of metallic foreign bodies, orthopaedic hardware, surgical clips and stents, pulmonary catheters and pacemaker wires. Streak artefact due to contrast in the vena cava can mimic a saddle embolus in the main pulmonary artery, or be mistaken for short segment thrombus in the upper lobe pulmonary arteries (Deva et al, 2008)

Superior vena cava streak artefact can be minimised by administration of a saline bolus following injection of intravenous contrast (Somanathan and Saade, 2012: 5).

Linear streak artefact causes pseudo-filling defects, which may be recognised on coronal or sagittal reformatted images by sharp horizontal upper and lower edges parallel to the scan plane (Deva, et al, 2008).

Photon starvation artefact

In patients with increased body habitus, photon attenuation increases exponentially with increasing patient thickness resulting in excessive quantum mottle and photon starvation artefact. Inadequate photons reaching the detectors result in reduced signal to noise and contrast to noise ratios, and generally degraded image quality. Radiation dose needs to be increased to counteract this (Yeo, Zhou and Lim, 2017:22). It is recommended that patients with an increased body mass index should be scanned at 120 kVp for CT angiographic studies (Modica, Kanal and Gunn, 2011:819). Iterative reconstruction technique may also be used minimise

image noise. Larger collimation or thicker reconstructed slices also helps to increase signal to noise ratio in larger patients (Palacio *et al.*, 2015:220).

1.2.3. Patient factors influencing CTPA image quality

There are multiple patient related factors affecting diagnostic quality of CTPA studies, and pulmonary arterial contrast enhancement in particular. This includes body habitus and venous anatomy, pregnancy and hyperdynamic circulatory states, dyspnoea, respiratory distress and parenchymal lung disease, cardiac dysfunction, shock and hypotension, congenital cardiac variants and pathology.

Contrast flow and enhancement graph patterns generated during CTPA studies may even give early warning that a life threatening condition such as arrythmia or imminent cardiac arrest is present (Chaturvedi *et al.*, 2017: 127-128).

Vascular kinking, postoperative changes and presence of tumour may also change the arterial opacification pattern and mimic filing defects (Deva, et al, 2008). All of the above should be taken into account when planning and interpreting CT pulmonary angiographic studies.

1.3. Overview of previous research regarding CT pulmonary angiography image quality and impact on diagnostic yield.

The following section reviews previous research relating to CTPA image quality, dose, technique and impact on diagnostic yield. Literature on the role of retrospective review and audit in radiology quality assurance programs is included.

1.3.1. Previous research investigating technical aspects of CTPA image quality

Published research investigating CTPA image quality and the effect of main pulmonary outflow tract opacification on diagnostic outcome.

Boston based thoracic radiologists Wittram and Jones have published extensively on the topic of CT pulmonary angiography image quality, and their work is frequently cited in later papers (Wittram, 2007) (Jones and Wittram, 2005). During 2005, they

published a large retrospective image quality review of 3612 CT pulmonary angiograms, of which 237 was deemed ‘indeterminate’. Findings were statistically evaluated and compared with patient outcome. The incidence of indeterminate studies at their institution was 6. 6%. This was deemed comparable with published literature of 10 studies with a range of percentages from 0.5% to 10.8% (mean of 6.4%) (Jones and Wittram, 2005: 337).

In their study, radiology reports were evaluated to find reasons for the indeterminate outcomes, including respiratory motion artefact, inadequate contrast enhancement, image noise due to large body habitus, lung parenchymal changes, streak artefact and multiple or no reasons (Jones and Wittram, 2005: 334).

The level where the pulmonary arterial tree could be evaluated with certainty was determined, and it was noted if patients had any follow up imaging. Thereafter the author reviewed images of these indeterminate studies, and a control group of 25 randomly selected studies, for pulmonary embolism, contrast attenuation in the MPA, motion artefacts, image noise and flow artefacts. Attenuation in the main pulmonary outflow tract was measured by placing a region of interest (ROI) measuring at least half the diameter of the artery over the largest image of the main pulmonary artery. Optimal opacification at this level was defined as at least 250 HU at their institution. They also noted the presence of pulmonary pathology, and any technical factors related to contrast administration. Finally, they compared the subjective findings as stated in the radiology reports with objective imaging findings and correlated with patient outcome by reviewing electronic medical records. They concluded that motion artefact occurred in 74.3% of the indeterminate studies, and poor opacification in 39.7%. Beam hardening, streak artefact and image noise were infrequent reasons for non-diagnostic outcome (Jones and Wittram, 2005: 332).

It is, however, to be noted that imaging during this 2005 study was acquired on older 4 or 16 detector row CT scanners, and that motion artefact may be less common now with modern advances in technology. Bolus tracking technology was also not used to initiate scanning during this study, as is most commonly practiced presently. The authors suggest that optimising contrast administration could improve

attenuation rates in the main pulmonary outflow tract. The need for proper communication with clinicians and appropriate recommendations for follow up imaging is highlighted (Jones and Wittram, 2005: 334-335).

This original work has been replicated in some or other form by several other centres. Afzal et al (2015), performed an audit based at McMaster University, retrospectively reviewing CTPA studies performed at three hospitals over a 20-day period. Contrast opacification in the main pulmonary outflow tract was measured by placing a ROI occupying 50 % of the vessel over the main pulmonary artery. A value of 211 HU measured in the main pulmonary outflow tract was deemed adequate.
The audit target, based on previous literature, was to have less than 10 % of studies with pulmonary artery contrast opacification below this value (Afzal, Colapinto and Haider, 2015). Patient demographics and body habitus, as well as other quality parameters, such as the presence of artefacts and the use of validated clinical scoring systems (WELLS score and D-dimers.) were also evaluated. Their results varied widely between the three hospitals surveyed, from 1.5% through 9.5% to 12.3% CTPA studies with MPOT opacification below 211 HU. It was interesting to note that a validated clinical request scoring system was used at the hospital with the lowest number of indeterminate studies. This is probably due to higher pre-test probability of positive findings as determined by the Wells Score.

A New Zealand based study aimed to assess the incidence and aetiology of indeterminate CTPA studies (Yeo, Zhou and Lim, 2017). After consultation with an institutional biostatistician, images and reports of 403 studies, spanning a four-month period, were retrospectively reviewed. Studies were categorised as diagnostic, suboptimal and non-diagnostic based on the original radiology report, as well as retrospective radiological review of the images of the suboptimal or non-diagnostic studies by the authors. Suboptimal and non-diagnostic studies were deemed ‘indeterminate’ and possible causes explored. Patient demographics, technical scan parameters, average main pulmonary outflow tract contrast opacification and likely causes for indeterminate outcome were documented. It was noted whether further imaging was recommended in the radiology reports and lastly clinical outcomes of

the indeterminate group were explored further by reviewing the electronic case records.

In this study a rate of 6.6 % indeterminate CTPA studies were found to be comparable with published literature. Poor contrast opacification, motion artefact and increased noise due to patient body habitus emerged as main contributing factors. Poor contrast enhancement surpassed motion artefact as the most likely cause in this publication, probably due to the use of modern multislice scanners that minimised motion artefact. Timing of contrast administration and scan triggering was explored, as well as the effect of transient interruption of contrast due to vascular flow phenomena. The impact of patient factors, such as pregnancy and increased body habitus, was also assessed. Of concern was the finding that clinicians generally treated an indeterminate scan as 'negative', and the authors again highlighted the need for improved communication between reporting radiologists and treating clinicians (Yeo, Zhou and Lim, 2017: 22-23).

Studies with emphasis on radiation or contrast dose reduction

Other authors have focused on attempts to reduce radiation or contrast dose during CTPA imaging, while simultaneously maintaining or improving image quality (Yilmaz, 2013) (Chen *et al.*, 2017). With widespread utilisation of CTPA imaging and resultant increasing population radiation exposure, concern has been raised regarding stochastically increased risk for development of malignancy.

Yilmaz et al (2013) conducted a study prospectively comparing three different CT tube voltages (80 kVp, 100 kVp and 120 kVp) and the resultant image quality for 90 patients with suspected pulmonary embolism. No statistically significant difference in contrast enhancement or motion artefact was found in the three groups. The authors concluded that radiation dose was reduced up to 60% at lower voltages, which is particularly important for young female patients and those with a low pre-test probability of pulmonary embolism (Yilmaz, 2013: 913). At lower tube voltages, there is increased contrast opacification as well as increased image noise. The relative increase in noise is larger than the increase in contrast enhancement. Despite the resultant decline in the signal to noise ratio, image quality is maintained. This is because of increased photo-electric effect at low voltages, which allows better

exploitation of the K-edge of iodine, which is 33.2 keV (Nania *et al.*, 2018: 320.E5). Reducing kV values from 120 kV or 140 kV to 80 kV increases X-ray attenuation 1.6 to 2 times respectively (Yilmaz, 2013: 912).

Chen et al (2017: 649) has proven that radiation dose can be significantly reduced by lowering kVp settings, and image quality maintained or improved despite the resultant increase in noise. These authors retrospectively reviewed scans that had already been performed according to standard diagnostic need and imaging protocols. CT tube voltage (kVp), tube-current time product (mAs) and radiation dosage in dose length product were recorded. Image quality was assessed by manual measurement of main pulmonary artery contrast opacification in Hounsfield Units, and assessment of image noise calculated using the standard deviation of density in the main pulmonary artery.

Images were subjectively rated for diagnostic quality by an experienced radiologist blinded to the technical scanner settings, using an ascending 5-point scale, ranging from 1= non-diagnostic, 2 = diagnostic but poor quality, 3 = average quality, 4 = good quality, 5 = excellent (Chen et al, 2017: 649). Patient size was estimated using a transverse chest diameter measured on the CT scan scout view, using a cut -off value of 35 cm to classify patients into ‘larger’ and ‘smaller’ groups, with chest measurement ≥ 35 cm or < 35 cm respectively.

In this study, contrast opacification in the main pulmonary artery was again used as an objectively measurable surrogate for image quality. It was found that reducing the tube voltage significantly reduced radiation dose. Simultaneously increased main pulmonary artery contrast opacification offset the slight increase in image noise, with resultant overall improvement in image quality. The authors concluded that reducing tube voltages from 120 kVp to 80 kVp resulted in reduced radiation dose whilst improving both subjective and objective measurements of image quality, even in large patients (Chen et al, 2017: 650). Image reconstruction techniques was shown to reduce image noise and further enhance quality (Chen et al, 2017: 651-652).

Nania et al (2018) conducted an audit focusing on dose length product, diagnostic reference levels and effects on imaging outcome. They found the average dose length product at their Edinburg institution to be higher than local and national diagnostic reference levels (Nania *et al.*, 2018: 320.E3). Following their research, a new protocol was subsequently introduced, bringing their department in line with internationally benchmarked lower radiation doses whilst maintaining adequate image quality.

Other authors have studied the effect of a decrease in dose of intravenous radiographic contrast media during CTPA imaging, with a view to minimising adverse effects related to contrast administration, while achieving adequate image quality (Assi and Abu Arra, 2017). Although contrast induced nephropathy may be less concerning then originally suggested, it remains relevant in diabetic patients, those with pre-existing impaired renal function and atopic patients. The effect of iodated contrast on the thyroid is also not yet fully understood (Hendriks *et al.*, 2016:7).

In the Netherlands, Hendriks et al (2016) studied the effect of individually tailored contrast enhancement in a group of one hundred patients undergoing CTPA for suspected pulmonary embolism. The focus of their study was the effect that the total amount of injected iodine, as well as the injection rate, had on pulmonary artery contrast enhancement and image quality. In this prospective study, they compared 50 patients undergoing CTPA according to standard protocols with a fixed dose of intravenous contrast, with a group of 50 where contrast dose and flow rate were individualised based on body weight. Images were immediately reviewed by radiologists, who scored it subjectively using a four-point Likert scale (Grade 1 = non-diagnostic, 2 = diagnostic, 3 = good, 4 = excellent image quality) and objectively by measuring contrast opacification in the pulmonary arterial system. Main pulmonary artery density measurement of 180 Hounsfield units was used as cut-off value to define an adequately enhanced diagnostic study. They found that lower doses of contrast media were administered in the individualised group, while image quality was preserved or improved (Hendriks *et al.*, 2016).

Experimental research evaluating the effect of respiratory breath hold techniques on pulmonary artery contrast enhancement

A retrospective analysis of 520 CTPA examinations, half of which were performed after deep inspiration followed by breath holding and half during breath holding alone, found that eliminating the deep inspiration technique reduced the number of scans with suboptimal opacification of the pulmonary artery, defined as <150 HU in this study (Kay *et al.*, 2014).

Another study showed that non-diagnostic CTPA studies with inadequate pulmonary artery contrast enhancement can be salvaged by rescanning in the expiratory phase, thereby limiting the effect of transient attenuation artefact (Chen *et al.*, 2008). This artefact is caused by negative intrathoracic pressure during inspiration and resultant inflow of un-opacified blood from the inferior vena cava into the right heart, mimicking filling defects in the pulmonary arterial tree (Chen *et al.*, 2008: 166).

In their study, 18 patients with indeterminate CTPA studies during inspiration were rescanned in expiratory phase, obtaining adequate contrast opacification and upgraded diagnostic outcome in all cases.

1.3.2. Role of retrospective audit in radiology quality assurance

Radiologists have a responsibility to conduct regular quality assurance (QA) programs (Chen et al, 2017: 649) to ensure patient safety, limit unnecessary radiation exposure and ensure reliable diagnostic imaging. The European Society of Radiology (ESR) perspective is that participation in clinical audit demonstrates commitment to the delivery of a high quality service and may indicate areas of the service where further investment is required (ESR Subcommittee on Audit and Standards, 2010). The British Royal College of Radiology has established a Clinical Radiology Audit Committee, and an associated website titled Auditlive, supplying various clinical audit templates, including the topic of CTPA image quality (Muller and Beattie, 2013). A Kenyan study assessed radiological quality assurance at a national level. It was determined that adherence to quality assurance programs in Kenya was reasonable, but with room for improvement, especially regarding radiological equipment performance and image quality. The authors conclude that developing countries should establish adequate guidelines and legal frameworks for

QA and QC programs of medical imaging equipment and procedures, ideally matching standards in developed countries (Korir *et al.*, 2013).

1.4. Retrospective review of CTPA image quality at Groote Schuur hospital

This study investigated image quality of CTPA studies performed for diagnosis of pulmonary embolism at Groote Schuur hospital, focusing on the incidence of indeterminate studies and subsequent diagnostic outcome. Like the majority of studies addressing this topic in the published literature, this research was conducted retrospectively, by reviewing radiology requests, images and reports of studies that had already been performed based on clinical diagnostic need. Data was obtained by accessing the radiology information system (RIS) and picture archiving and communication system (PACS), reviewing consecutive studies over a six-month time period.

The study followed from the seminal work by Wittram and Jones as cited, as well a CTPA audit review template from the Auditlive website of the British Royal College of Radiology and other published studies based on the above (Jones and Wittram, 2005), (Muller et al, 2013), (Yeo, Zhou and Lim, 2017). A UK study followed a similar approach, however, comparing the CTPA imaging performance of three medical facilities (Afzal, Colapinto and Haider, 2015). CTPA image quality of consecutive CTPA studies performed at Groote Schuur Hospital was evaluated retrospectively.

Figure 1-7 illustrates the conceptual model used in this research, demonstrating the complex relationship between health risk and technical factors on CTPA image quality, and effect on diagnostic and clinical outcome. Adequate contrast opacification in the Main Pulmonary Outflow Tract was identified as an objectively measurable and potentially modifiable benchmark for CTPA image quality. As in the aforementioned studies it was used as a proxy for image quality in this research.

Motion artefact, which was a major problem historically, should decrease in importance with advances in scanner technology. The presence of motion and streak artefact was, however, also noted as secondary factors that affect image quality. Although this was not the main focus, the study also noted the relationship between

patient health risk factors, effective dose, image quality and subsequent diagnostic and clinical outcomes.

CTPA studies at Groote Schuur are performed according to a standardised protocol. Radiation and contrast dose reduction, specific methods of contrast administration or respiratory manoeuvres during scanning has not been the focus of this study.

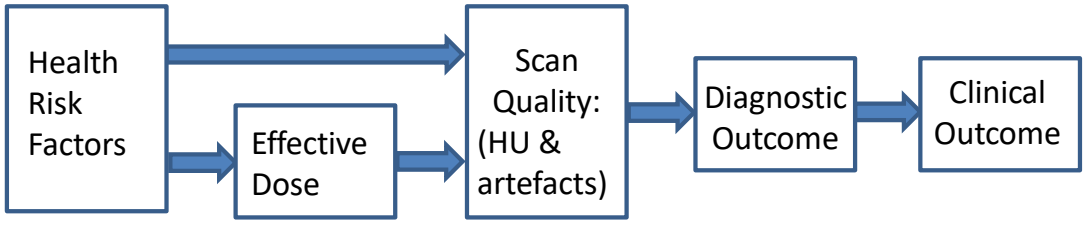

Figure 1-7: Conceptual model used in this research.

1.4.1. Motivation of research

As highlighted in section 1.1.1, pulmonary embolism is the third most common cause of cardiovascular death worldwide, and leads to considerable morbidity and mortality. Accurate diagnosis is important in guiding clinical management, and hinges heavily on imaging, as clinical findings are often non-specific. CT pulmonary angiography is commonly requested for this indication, but can be technically challenging to perform, as discussed in section 1.1.3

Reporting radiologists at Groote Schuur hospital sporadically encounter CTPA studies where image quality is deemed suboptimal, leading to indeterminate results and precluding definitive diagnosis. This may lead to increased patient exposure to radiation and contrast material, as well as additional cost, due to repeat studies. Subsequent additional imaging may need to be requested, or empirical therapy instituted with associated risk of adverse reactions. As discussed, indeterminate studies may also be misinterpreted as negative by treating clinicians, with potentially fatal consequences.

International best practice mandate regular audits and quality reviews for imaging departments (ESR Subcommittee on Audit and Standards, 2010). This research was conducted in order to benchmark CTPA image quality at the Groote Schuur Hospital Radiology department against published standards and explore the effect of image quality on diagnostic outcome.

2. MATERIALS AND METHODS

2.1. Research Problem Statement

The basic premise of this research was that inadequate CTPA image quality leads to diagnostic uncertainty for the reporting radiologist, and possibly the clinician. This is unacceptable when the imaging is acquired to rule out potentially life-threatening conditions such as pulmonary embolism. The research retrospectively assessed the image quality of CTPA performed at Groote Schuur hospital. The proportion and causes of indeterminate studies, and effect on diagnostic and clinical outcome, was investigated. Insights gained led to suggestions for improved CTPA technique and future research, with the aim of increasing diagnostic certainty.

2.2. Study objectives

The main objective of this research was to retrospectively assess the image quality of CTPA studies performed at Groote Schuur hospital over a six-month period.

2.2.1. Research aims

The research aims to benchmark quality of CTPA imaging performed at Groote Schuur hospital for pulmonary embolism by evaluating the following aspects:

a. Objective measurement of contrast opacification in the main pulmonary artery
b. Percentage of radiology reports where the diagnostic outcome was indeterminate.

2.2.2. Research questions

The following was the main research question answered in this study:

What was the relationship between CTPA image quality and diagnostic and clinical outcomes, as well as related variables such as health risk factors and effective dose?

The above research question has been broken down into the following sub-questions:

1. Using contrast opacification in the main pulmonary outflow tract as the main determinant for image quality, as explained in Section 1.3.1, in what

percentage of studies was the density measurement below the cut-off value (< 211 Hounsfield units)?

2. How did the presence of artefacts contribute to image quality and diagnostic outcome?
3. In what percentage of radiology reports was the diagnostic outcome indeterminate?
4. What was the relationship between inadequate contrast opacification and diagnostic outcome?
5. How did patient demographic and health risk factors contribute to image quality and diagnostic outcome?
6. What was the relationship between health risk factors and effective dose?
7. What was the relationship between diagnostics findings and mortality/ clinical outcome?

2.3. Research paradigm

This is a retrospective, quantitative, cross-sectional, single centre review of CTPA image quality at an urban tertiary Level 3 academic hospital. The study was conducted in the Groote Schuur Hospital Radiology Department. Ethical approval to conduct the study was obtained from the Faculty of Health Sciences Human Research Ethics Committee of the University of Cape Town (HREC reference number: 520/2019) and the hospital. We reviewed electronic clinical CT requests, radiology reports, electronic laboratory records and digital images stored on a Picture Archiving and Communication System. Our study was not randomised.

2.4. Selection criteria

All patients, aged 18 and older, who underwent Computed Tomography Pulmonary Angiography for suspected acute or chronic pulmonary embolism at the Groote Schuur Hospital Radiology Department during the study period were included. Data was collected for a six-month period spanning from 01 July 2018 until 31 December 2018.

2.4.1. Inclusion criteria

a) Consecutive CTPA studies, requested to confirm a suspected diagnosis of acute or chronic pulmonary embolism within the above time period, were included.

2.4.2. Exclusion criteria

a) CTPA studies where standard protocol could not be followed due to the presence of renal disease, contrast allergy or other factors were excluded.
b) CTPA studies performed on adolescents younger than 18 years were excluded.
c) Imported images from CTPA scans performed at other hospitals were excluded.

2.5. CT Pulmonary Angiography

During the research period, Computed Tomography Pulmonary Angiography at Groote Schuur hospital was performed on one of two machines: A Toshiba Aquilion Prime-160 Series 160 slice helical CT Scanner. (Toshiba Medical Systems, Okinawa, Japan) and a SOMATOM go.Top 128 Slice scanner (Siemens Healthineers, Erlangen, Germany).

Images were obtained after administration of 100 ml of low osmolality iodated intravenous contrast (Omnipaque) via an automated pump injector, through an 18- or 20-gauge cannula, using a standard CTPA protocol in helical mode at 120 kVp. A pre-contrast planning scan was performed over the carina and the chosen level for the main pulmonary artery. The region of interest (ROI) was placed over the trunk of the main pulmonary artery.

Threshold trigger of pulmonary trunk contrast opacification was set at 100 HU for the Siemens scanner, and 180 HU for the Toshiba machine, with immediate triggering. Patients were instructed to inspire deeply. The scan range was from the diaphragm to lung apices.

2.6. Data collection

Data collection was performed by using the modality search function of the existing Phillips XIRIS 8.2 15.4 Radiology Information System and Phillips Intellispace Picture Archiving and Communication Systems.

Consecutive CTPA images were retrospectively viewed on Hewlett Packard workstations and Barco Diagnostic monitors, using Phillips Intellispace software and the Phillips Isite plugin.

Axial 3 mm reconstructions were obtained in the soft tissue and lung windows:

- Soft tissue window: window width/ window level 500/70 HU
- Lung window: Window width/ window level 1600/-550 HU

Objective measurement of contrast opacification in the MPOT was obtained by scrolling on axial images in the soft tissue window, selecting the image slice with the widest view of the main pulmonary artery and placing the ROI to cover at least 50% of the diameter. Reliability was ensured by calculating the mean of two measurements, using the same standard measurement technique in every case.
Adequate contrast opacification of the pulmonary trunk was defined as average HU value greater than or equal to 211, based on previously published theoretic minimum attenuation values to see both acute and chronic pulmonary venous thrombo-emboli (Wittram, 2007). The maximum diameter of the MPOT, as well as contrast opacification in the ascending aorta, was measured in similar fashion on the same axial slice.

Subjective review for the presence or absence of significant motion or streak artefact was performed utilising both soft tissue and lung windows. Shoulder measurement on the scout scanogram was taken as a proxy for body habitus, with a shoulder measurement ≥35 cm defining a large patient, as in a previous study exploring the relationship between patient body habitus, image quality and radiation dose (Chen *et al.*, 2017). Radiation dose-length product (DLP) was documented. Effective dose was calculated from the DLP using published conversion factors (0.014 for chest in adults) (Yeo, Zhou and Lim, 2017).

Specific data and patient variables were extracted from the clinical requests and radiology reports as determined by the investigators. The indication for the study was recorded as suspected acute or chronic pulmonary embolism.

Parameters such as age, gender, inpatient or outpatient status and risk factors for pulmonary embolism such as malignancy, HIV, recent surgery, pregnancy or cardiovascular disease were recorded.

Diagnostic outcome was classified as conclusive (either positive or negative for pulmonary embolism) or indeterminate based on the findings of the reporting radiologist. Studies where the presence or absence of pulmonary embolism up to the segmental level could be confirmed were deemed conclusive. Indeterminate studies were those labelled inconclusive, suboptimal, non-diagnostic or where qualifying statements were included in the report. Alternative or additional diagnostic CT findings were also documented, classifying them in broad groups, for example other pulmonary, cardiac, infective and malignant conditions.

Lastly mortality status at 1, 3 and 6 months after study acquisition date was assessed where available by evaluating hospital information system records and subsequent imaging requests or lack thereof. Records of the 30 patients with indeterminate scan outcomes were reviewed in order to assess the potential impact of diagnostic uncertainty on clinical decision making and management.

2.7. Statistical analysis

The collected data were entered into a computerised Excel spreadsheet for review. Basic descriptive statistical analysis was performed, including calculation of percentages, averages and mean values. Contrast opacification measured in Hounsfield units, was evaluated both as a continuous variable and a categorical variable (using the threshold of 211 HU as adequate), but it was decided to only include the categorical variable in the results.

Data analysis was performed using SPSS Version 26. Pearson's correlations were used to investigate relationships between continuous variables, independent sample t-tests were used to compare differences in a continuous dependent variable and a categorical independent variable, and chi-square tests were used to investigate associations when both variables were categorical. The level of significance was set at $\alpha = 0.05$.

3. RESEARCH RESULTS

This section presents the results of the research. Section 3.1 describes the demographic characteristics of the sample. Thereafter section 3.2 looks at the image quality and diagnostic outcome of the CTPA studies and section 3.3 comments on clinical and mortality outcome.

3.1. Sample description, demographics and clinical factors

A total of two hundred and thirty-one (231) patients were identified as having a CTPA study performed for suspected pulmonary embolism during the six-month study period from 1 July 2018 to 31 December 2018. The scans of two patients under the age of 18 were excluded. Two studies were excluded as scans were performed at outside hospitals and images imported to Groote Schuur Hospital PACS. One scan was excluded as no images were attached to the accession number. This left two hundred and twenty-six (226) CTPA studies that were included in the study.

3.1.1. Demographics

The age of patients in the sample ranged between 19-84 years, with an equal distribution amongst age categories as shown in Figure 3-1 below. Mean age was 46.9 years (SD=17.64), and the median age was 45 years.

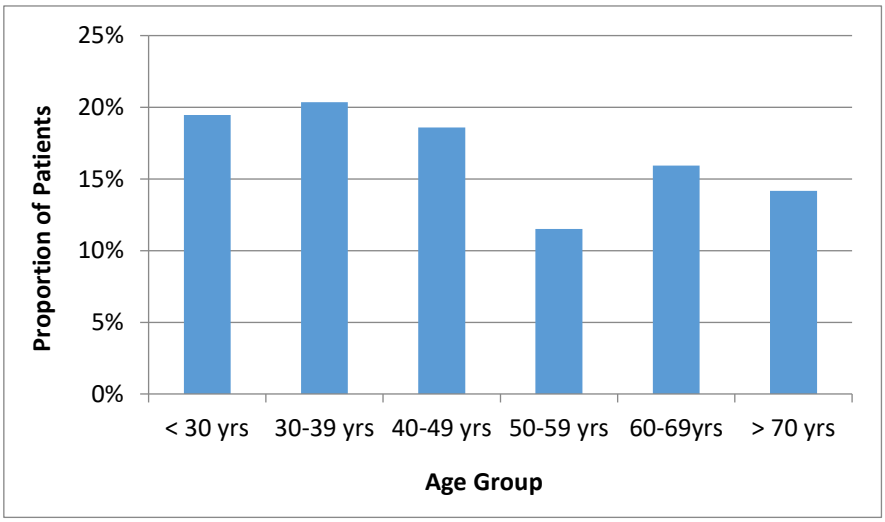

Figure 3-1: A breakdown of sample patients according to age groups.

It was interesting that most of the study population comprised females.
There were 69 % (N=156) females and 31% (N=70) males.

3.1.2. Health risk factors

In addition to age, gender and pregnancy status, known health risk factors for pulmonary embolism were identified as demonstrated by Figure 3-2 below:

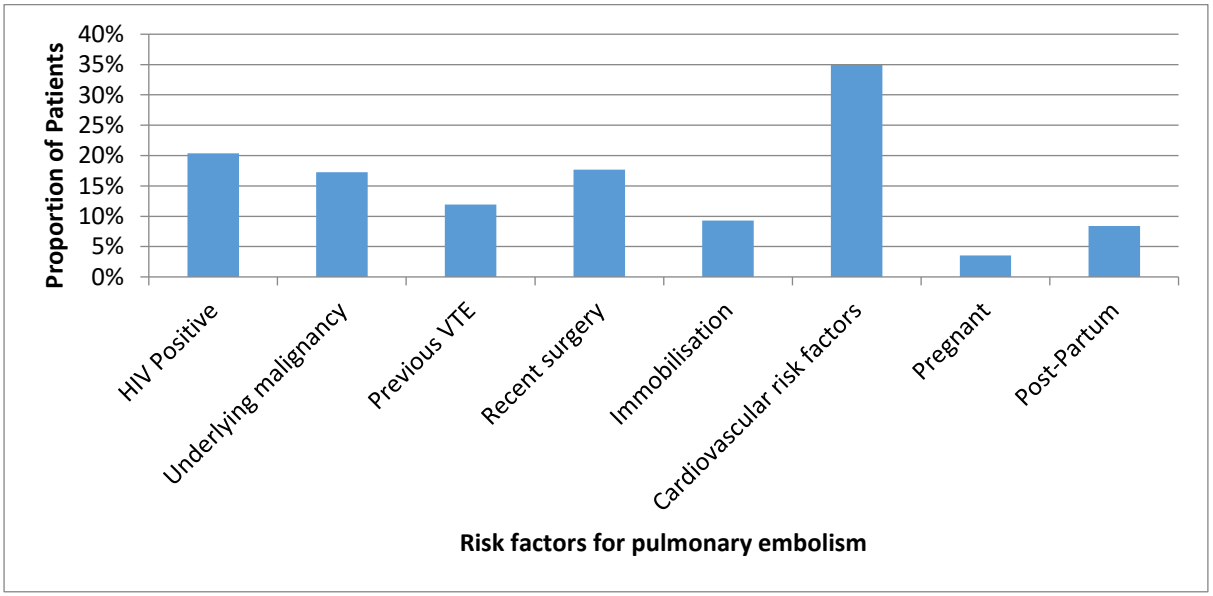

Figure 3-2: Health risk factors for pulmonary embolism.

20 % of patients were HIV positive (N=46). Underlying malignancy was present in 17 % (N=39) and previous VTE in 12% (N=27). Cardiovascular risk factors were observed in 35% (N=79). Recent surgery was performed in 18% (N=40) of cases and immobilisation was deemed a risk factor in 9 % (N=21) of cases. 4 % (N=8) of all patients were pregnant and 8 % (N=19) post-partum. The majority were neither pregnant nor postpartum.

At least one medical risk factor was identified in 40.71% (N=92) of patients, with more than one risk factor present in several patients as summarised in Figure 3-3 below.

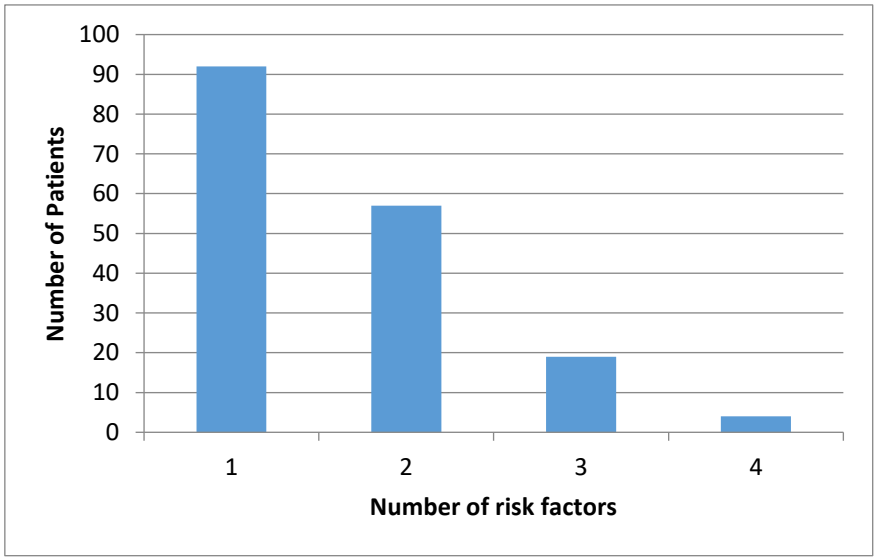

Figure 3-3: Number of patients with one or more health risk factor.

Scanogram shoulder measurement was used to estimate patient body habitus, with a measurement of ≥35 cm defining a large patient. Out of the 226 patients, 42 % (N=96) had scanogram shoulder measurements ≥ 35 cm.

The vast majority were inpatients, comprising 89 % (N=202), with only 11 % (N=24) of the sample consisting of outpatients. 87 % (N=196) of scans were performed for suspected acute pulmonary embolism. Only 13 % (N=30) were requested for chronic thromboembolism. Patients who had suspected acute pulmonary embolism were mainly inpatients (183/202; 90.6 %).

Compared to inpatient scans requested for chronic thrombo-embolism (19/202; 9.4 %), a statistically higher proportion of outpatient scans (11/24; 45.8%) were requested for suspected chronic thromboembolism (χ^2 = 24.73, p <.001, Cramer's V = 0.33). Overall, D-Dimer tests were performed in only 26% (N=58) of the 226 cases, but in 21 % (N = 5) of out-patients.

3.2. Image quality and diagnostic outcomes

3.2.1. Summary of image quality and diagnostic outcomes

Table 3-1 Summary of results relating to MPOT contrast opacification and diagnostic outcome.

Contrast opacification range	PE diagnostic outcome		Total
	Conclusive	Indeterminate	
≥ 211 HU	83.63 % (N=189)	6.64 % (N=15)	90.27% (N=204)
< 211 HU	3.10 % (N=7)	6.64 % (N=15)	9.73% (N=22)
Total	86.73 % (N=196)	13.27 % (N=30)	

Note: Percentage values calculated as percentage of total number of studies (N=226).

Minimum MPOT contrast opacification required to identify acute and chronic thrombi was defined as 211 HU based on published literature. As shown in Table 3-1, this standard was met in 90.3 % (N=204) of the 226 studies that we reviewed. Inadequate contrast opacification measuring < 211 HU was identified in 9.7 % (N=22) of CTPA studies performed during the study period.

In the sub-group where opacification measured ≥ 211 HU, 93 % (189 out of 204) of patients had a conclusive outcome. In comparison, in the sub-group where opacification measured < 211 HU, a significantly smaller percentage of 32% (7 out of 22) had a conclusive outcome. Statistical analysis using the chi-square test confirmed that a conclusive outcome was significantly more likely when the contrast opacification was ≥ 211 HU ($\chi^2 = 63.83$, $p < .001$, Cramer's $V = 0.53$).

3.2.2. Analysis of technical factors affecting CTPA image quality

Table 3-2 below analyses the occurrence of motion and streak artefacts in CTPA scans with contrast opacification above and below the threshold of 211 HU, and for indeterminate and conclusive outcomes. The table also lists the average contrast opacification and p-value of each category grouped according to observed artefacts.

The main observation is that by far the majority of studies (189 out of 226) were conclusive with MPOT contrast opacification ≥ 211 HU. Of this group 59.79 % (113/189) had no streak or motion artefact. The remaining 40% was conclusive despite having either motion or streak artefact or both. Note in Table 3-2 that there

were 32 studies that had both motion and streak artefacts and that values in this row were subtracted in calculating (sub-)totals.

The 30 studies with indeterminate outcome were equally divided in two groups with contrast opacification above and below the 211 HU threshold. All 15 studies in the group that had an indeterminate outcome, but adequate MPOT contrast opacification ≥ 211 HU, had artefacts. Of these, 6 had borderline contrast opacification between 211 and 250 HU, with some values just above the threshold e.g., 213 HU or 218 HU.

In the 15 studies with indeterminate outcome and low contrast opacification < 211 HU, motion or streak artefact or both contributed to poor image quality in nine cases. For the six out of 15 without motion and streak artefacts, low contrast attenuation alone made the scan uninterpretable. Seven CTPA scans were conclusive despite contrast opacification below the threshold of 211 HU. One of these scans were positive for pulmonary embolism, with large lobar and segmental filling defects clearly visible regardless of low attenuation in the pulmonary arterial system. In most of the other cases, a clear alternative CT finding could account for the clinical presentation of the patient, for example large pulmonary metastases or lobar pneumonia, likely increasing the diagnostic confidence of the reporting radiologist.

Table 3-2: Technical analysis of CTPA scans categorised according to PE diagnostic outcome (i.e., conclusive or indeterminate) and contrast opacification range (i.e., above or below the threshold value of 211 HU).

Artefact	PE diagnostic outcome				Total	Average Contrast Opacification (HU)	p-value
	Conclusive		Indeterminate				
	<211	≥211	<211	≥211			
Motion	0.88 % (N = 2)	24.34 % (N = 55)	2.65 % (N = 6)	5.75 % (N = 13)	33.62 % (N = 76)	329.01 HU	0.022
Streak	0.88 % (N = 2)	19.47 % (N = 44)	2.65 % (N = 6)	3.10 % (N = 7)	26.10 % (N = 59)	313.23 HU	0.002
No artefact	1.76 % (N = 4)	50.00 % (N = 113)	2.65 % (N = 6)	0 % (N = 0)	54.41 % (N = 123)	367.34 HU	0.042
Minus: Motion and Streak	0.44 % (N = 1)	10.18 % (N = 23)	1.33 % (N = 3)	2.21 % (N = 5)	14.16 % (N = 32)	312.48 HU	0.034
Total	3.10 % (N = 7)	83.63 % (N = 189)	6.64 % (N = 15)	6.64 % (N = 15)			

3.2.3. Analysis of diagnostic outcome

Conclusive CTPA studies include positive scans where pulmonary embolism could be confirmed, as well as negative studies where pulmonary embolism could be excluded up to segmental level by the reporting radiologist. For indeterminate studies pulmonary embolism could not be confirmed or excluded with confidence by the reporting radiologist.

Diagnostic outcomes related to pulmonary embolism

Pulmonary embolism was confirmed in 22% of patients (N=50) and excluded in 65 % (N=146) of the 226 scans reviewed over the study period. There were 30 indeterminate scans, comprising 13% of the total, where the reporting radiologist could not confidently confirm or exclude pulmonary artery filling defects up to the segmental level (see Table 3-3).

Table 3-3: CTPA diagnostic outcome relating to pulmonary embolism and additional or alternative findings.

Diagnostic finding detail	PE diagnostic outcome		
	Positive PE	Negative PE	Indeterminate
PE only	6.19 % (N=14)	----	----
PE & additional finding	15.93 % (N=36)	----	----
Alternative finding present	----	58.41 % (N=132)	10.62 % (N=24)
No alternative finding present	----	6.19 % (N=14)	2.65 % (N=6)
Total	22.12 % (N=50)	64.60 % (N=146)	13.27% (N=30)

Additional or alternative diagnostic CT findings

Importantly, additional or alternative diagnostic CT findings were present on the majority of scans, as shown in Table 3-3.

Figure 3-4 demonstrates frequency distribution of broadly categorised CT findings. These included pulmonary embolism in 22% (N=50), infection in 33% (N=74), other

pulmonary findings in 29% (N=65), malignancy in 8% (N=18) cardiac findings in 21% (N=47), and pulmonary hypertension in 11% (N=25).

'Other' significant CT findings in 1% of patients (N=3), were an ectopic thyroid compressing the airway, tracheal stenosis and a right common iliac vein DVT. No significant CT diagnosis could be made in 9% (N=20) of CTPA studies performed over the six-month period. Several findings were sometimes present in the same patient, for example pulmonary embolism and malignancy, or infection and other pulmonary findings, therefore the percentages add up to a value greater than 100%.

Figure 3-5 shows that in the majority of cases (137 out of 226) only a single CT diagnostic finding was made, however, in a significant number of cases (i.e., 61) two diagnoses were made by the reporting radiologist.

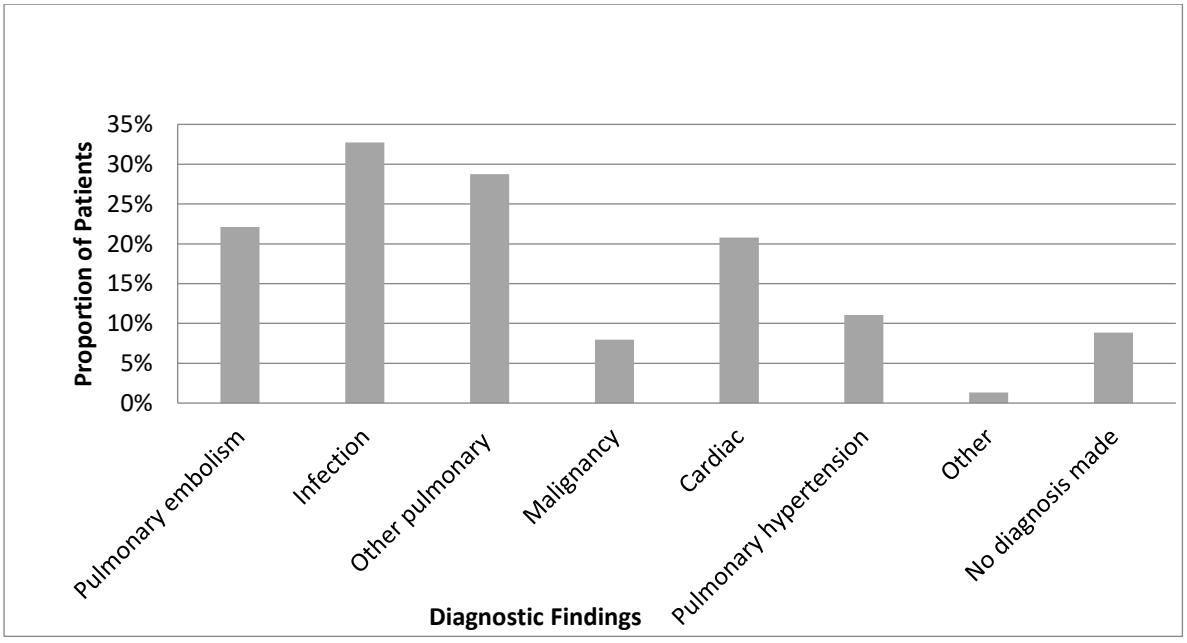

Figure 3-4: Frequency distribution of pulmonary embolism and other diagnostic CT findings.

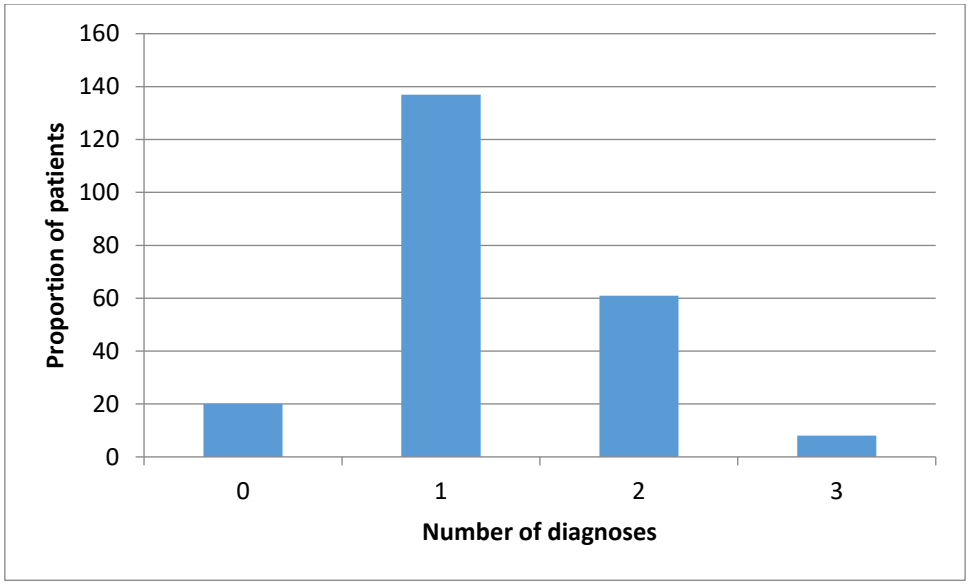

Figure 3-5: Proportion of patients with varying number of diagnoses.

Health risk factors and diagnostic outcome

Compared to patients without a surgical risk factor, patients who had undergone recent surgery were:

- significantly more likely to have an indeterminate PE finding (9/40; 22.5% vs 21/186; 11.3%),
- significantly less likely to have a positive finding for PE (4/40; 10% vs 46/186; 24.7%),
- equally likely to have a negative finding (27/40; 67.5% vs 119/186; 64%)

The statistical significance of the above was confirmed by a chi-square test result ($\chi^2 = 6.41$, p = 0.041, V = 0.17).

Effective dose, contrast opacification and diagnostic outcome

Patients in whom a conclusive PE diagnosis could be made had a significantly higher contrast opacification measured in HU, compared to those with an indeterminate PE diagnosis (t = -6.47, p < 0.001), but there was no difference in effective dose (t = 1.64, p = 0.103).

3.2.4. Statistical analysis of quantitative variables

This section includes statistical analyses investigating how health risk factors, effective dose, scan quality, diagnostic outcome and clinical outcome are related. Refer to Figure 1-7 for details of the conceptual model that is used in this research.

Note: For effective dose and contrast opacification (measured in HU), 2 outliers (scores > 3 *SD* above the mean) were removed from the data for analyses purposes. These deletions apply to the continuous variable HU but not the categorical HU variable.

Age was significantly correlated with contrast opacification (measured in HU) in the MPOT. Higher contrast attenuation values were measured in older patients.

Shoulder measurement was significantly correlated with both contrast opacification and effective dose. Lower average contrast opacification values (measured in HU) were measured in larger patients and they needed higher effective doses.

Average HU measured in the MPOT, and effective dose (ED) were also significantly correlated – patients with a higher contrast opacification values needed a lower effective dose (see Table 3-4).

Table 3-4: Pearson correlation analysis of continuous variables of the study.

				Variable Numbers		
Nr	**Variable**	**Mean**	**SD**	**1**	**2**	**3**
1	Age	46.92	17.64			
2	Shoulder measurement	33.30	5.73	0.02		
3	Average MPOT contrast opacification (HU)	355.75	125.18	0.24†	-0.36†	
4	Effective Dose	4.86	2.45	0.11	0.58†	-0.25†

†p < .001

Health risk factors and effective dose

Independent sample t-test compared effective dose between patients with and without various health risk factors. Effective dose did not differ statistically between those with and without the various health risk factors (all p-values > 0.05), except there was a trend in significance for HIV, with HIV negative participants needing a higher effective dose (Mean = 5.19 vs 4.41, t = 1.72, p = 0.089). Patients who were larger (shoulder measurements >35) needed a significantly higher effective dose (Mean = 6.47 vs 3.70, t= -10.03, p< 0.001).

Health risk factors and contrast opacification

Independent sample t-test compared average contrast opacification between patients with and without various health risk factors. As shown in Table 3-5, average opacification did not differ statistically between those with and without the various health risk factors (p- values > 0.05), except for the following: Patients who had previous surgery had a statistically lower average contrast opacification (Mean = 311.13 HU vs 365.46 HU, t= 2.52, p = .013). Patients with cardiovascular risk factors had a statistically higher average contrast opacification (Mean = 385.18 HU vs 340.34 HU, t= -2.58, p = .011). Patients who were larger (shoulder measurements >35 cm) had a statistically lower average contrast opacification (Mean = 321.46 HU vs 381.47 HU, t= 3.65, p < .001).

Table 3-5: Comparison of mean contrast opacification between patients with and without various health risk factors.

Health risk factor	Number of Patients (N)	Mean contrast opacification (HU)	t-value	p-value
HIV Positive?			-0.47	0.638
No	77	336.27		
Yes	45	347.09		
Underlying malignancy?			0.46	0.644
No	186	357.51		
Yes	38	347.18		
Recent Surgery?			2.52	0.013
No	184	365.46		
Yes	40	311.13		
Immobilisation?			0.72	0.471
No	203	357.70		
Yes	21	336.95		
Cardiovascular risk factors?			-2.58	0.011
No	147	340.34		
Yes	79	385.18		
Pregnant?			1.27	0.206

Health risk factor	Number of Patients (N)	Mean contrast opacification (HU)	t-value	p-value
No	127	368.42		
Yes	27	334.37		
Shoulder measurement > 35 cm?			3.65	0.001
No	128	381.47		
Yes	96	321.46		

Health risk factors and Image Quality

Chi-square tests were used to compare patients with and without risk factors and whether motion, streak, motion and streak, or no artefact was present in the image.

Larger patients (shoulder measurements > 35) were significantly more likely to have artefact present (38/96; 39.6% vs 33/130; 25.4%, $\chi^2 = 5.17$, p = 0.023, V = 0.15).

Patients with chronic PE were less likely to have motion artefact present (4/30; 13.3% vs 72/196; 36.7%; $\chi^2 = 6.38$, p = 0.012, V = 0.17), less likely to have streak artefact present (2/30; 6.7% vs 57/196; 29.1%; $\chi^2 = 6.78$, p = 0.009, V = 0.17), and more likely to have no artefact present (4/30; 13.3% vs 67/196; 34.2%; $\chi^2 = 5.25$, p = 0.022, V = 0.15).

Patients with a recent history of surgery were significantly more likely to have streak present (16/40; 40% vs 43/186; 23.1%, $\chi^2 = 4.86$, p = 0.027, V = 0.15). Patients with immobilisation were significantly more likely to have streak present (10/21; 47.6% vs 49/205; 23.9%, $\chi^2 = 5.55$, p = 0.018, V = 0.16), and more likely to have both motion and streak present (8/21; 38.1% vs 24/205; 11.7%, $\chi^2 = 10.91$, p = 0.001, V = 0.22). No other significant associations were found between health risk factors, including pregnancy, and image quality (all p-values > 0.05).

3.3. Clinical and mortality outcome

Table 3-6 below demonstrates the following: At 1-month from scan date, 169 patients were alive and 32 died missing data for 25 patients, at 3-months 148 were alive and 41 had died missing data for 37 patients, and at 6-months 133 were alive and 47 had died missing data for 46 patients.

As shown in the notes section of Table 3-6 below, there were significant associations between PE diagnostic outcome (Positive, Negative or Indeterminate) and Mortality at 1-month ($p = 0.041$), 3-months ($p = 0.049$) and 6-months ($p = 0.001$).

Post-hoc comparisons revealed the following: At 1-month, patients who were negative for PE were more likely to be alive compared to those positive for PE ($p = 0.012$), but there was no difference in mortality status between those negative and indeterminate for PE ($p = 0.728$), or between those positive and indeterminate for PE ($p = 0.181$).

At 3-months, patients who were negative for PE were more likely to be alive compared to those positive for PE ($p = 0.015$), but there was no difference in mortality status between those negative and indeterminate for PE ($p = 0.323$), or between those positive and indeterminate for PE ($p = 0.438$).

At 6-months, patients who were negative for PE were more likely to be alive compared to those positive for PE ($p < 0.001$), but there was no difference in mortality status between those negative and indeterminate for PE ($p = 0.320$), or between those positive and indeterminate for PE ($p = 0.115$).

There were no significant associations between contrast opacification (< or ≥ 211 HU) and mortality status at any of the 3 time points.

Table 3-6: Summary of mortality data for different PE diagnostic outcomes.

	PE diagnostic outcome			Total
	Positive PE	**Negative PE**	**Indeterminate**	
Mortality at 1-month (Note 1a)	13/47 (27.66 %)	15/126 (11.90 %)	4/28 (14.29 %)	32/201 (15.92 %) **(Note 2)**
Mortality at 3-month (Note 1b)	15/44 (34.09 %)	20/121 (16.53 %)	6/24 (25.00 %)	41/189 (21.69 %) **(Note 3)**
Mortality at 6-month (Note 1c)	20/42 (47.62 %)	21/116 (18.1)	6/22 (27.27 %)	47/180 (26.11 %) **(Note 4)**

Notes:

Note 1: Associations between PE Diagnostic Outcomes and Mortality are as follows:

a. At 1-month Chi-square (X^2 = 6.41, p-value = 0.041, Cramer's V = 0.18)
b. At 3-months Chi-square (X^2 = 6.04, p-value = 0.049, Cramer's V = 0.18)
c. At 6-months Chi-square (X^2 = 13.94, p-value = 0.001, Cramer's V = 0.28)

Note 2: Data missing for 25 patients.

Note 3: Data missing for 37 patients.

Note 4: Data missing for 47 patients.

Further review of the 30 indeterminate scans revealed the following:

Five patients appeared lost to follow up. In 20 out of 25 patients where records were available, an alternative CT diagnosis could be made. Clinicians interpreted 17 of these indeterminate CTPA studies as negative for PE, two as positive (anticoagulation started) and one as indeterminate with a subsequent V/Q scan demonstrating pulmonary emboli. Only five patients in this group died within the six-month period, all due to serious co-morbid conditions such as subdural empyema, endocarditis and sepsis.

In 5 of the 25 indeterminate CTPA scans, no alternative CT diagnosis could be made. Two of these CTPA studies were regarded as indeterminate by clinicians and subsequently confirmed positive for pulmonary embolism by V/Q scans. Three scans were regarded as negative and alternative diagnoses made based on clinical and laboratory findings. Out of this group no patient was confirmed to be deceased at 6 months after the scan.

4. DISCUSSION

This section contains the discussion, conclusion and recommendations following from the research.

4.1. Results in Context

This section presents an overall picture of the results as given in Section 3, in context of the literature, whilst addressing the study objectives as set out in section 2.2.

4.1.1. Summary of Results

The main findings of our study, that answer the different components of the research question, were the following:

1. *In what percentage of studies was the density measurement below the cut-off value (< 211 Hounsfield units)?* (Refer to section 4.1.2)
    a. Inadequate MPOT contrast opacification was reported in 9.7 % of studies, which was better than 10.8 % that was the audit target in previous research.
2. *How did the presence of artefacts contribute to image quality and diagnostic outcome?* (Refer to section 4.1.3)
    a. Motion and/ or streak artefact occurred in 45.6 % of studies.
    b. As found in previous research, motion artefacts were the most common artefact, occurring in 33.62 % of studies.
    c. In comparison streak artefacts were seen in 26.10 % of studies.
    d. Motion and streak artefacts occurred concurrently in 14.16 % of studies.
    e. Artefacts were present in 80 % of the 30 indeterminate studies, but only in 40% of the 196 conclusive studies.
    f. In indeterminate studies with contrast opacification below the threshold, a higher percentage of studies had artefacts compared with literature.
3. *In what percentage of radiology reports was the diagnostic outcome indeterminate?* (Refer to section 4.1.4)
    a. The percentage of indeterminate studies was 13.3% versus 6.4% in literature.

b. 22% of the studies were positive for pulmonary embolism versus 20% in literature.
c. Alternative or additional CT radiological diagnoses were made in 85 % of studies in this research.

4. *What was the relationship between inadequate contrast opacification and diagnostic outcome?* (Refer to section 4.1.5)
    a. In indeterminate studies contrast opacification was below the threshold in 50% of studies, which is similar to a previous study.
    b. A statistically significant association was found between adequate MPOT contrast opacification and a conclusive diagnostic outcome
5. *How did patient demographic and health risk factors contribute to image quality?* (Refer to section 4.1.6)
    a. Patients with chronic thrombo-embolism were found to be statistically less likely to have motion artefacts.
    b. Patients with recent history of surgery statistically more likely to have streak artefacts present.
    c. Patients with immobilisation were statistically more likely to have both motion and streak artefacts present.
    d. Patients with a recent history of surgery had a statistically lower, and those with cardiovascular risk a statistically higher MPOT contrast opacification.
    e. As in literature, increased body habitus was identified as a contributing factor to suboptimal image quality.
6. *How did patient demographic and health risk factors contribute to diagnostic outcome?* (Refer to section 4.1.7)
    a. The only health risk factor that made a positive PE finding statistically significantly less likely was recent surgery.
7. *What was the relationship between health risk factors and effective dose?* (Refer to section 4.1.6)
    a. Patients who were larger (shoulder measurements >35 cm) needed a statistically significantly higher effective dose.
8. *What was the relationship between diagnostics findings and mortality/ clinical outcome?* (Refer to section 4.1.8)

a. Patients with a positive diagnosis of PE had a higher mortality rate at all three endpoints (i.e., one, three and six months after the scan), compared to patients with negative and indeterminate scans.
b. It was found that clinicians interpreted indeterminate scans as being negative, however, it was surprising that in our research this did not impact adversely on mortality.

4.1.2. Contrast Opacification below Threshold

Based on published literature, a threshold of 211 HU has been identified as the minimum contrast opacification in the MPOT that allows diagnosis of both acute and chronic pulmonary emboli. Values of 250 HU or above are deemed optimal. In our research, adequate contrast opacification was demonstrated in 90.3% of 226 consecutive CTPA studies over a six-month period. Inadequate MPOT contrast opacification (below the threshold of 211 HU) occurred in 9.7% (N=22). This is better than the audit target of < 10.8 % as set by Afzal et al (2015) in their UK based audit of CTPA image quality.

4.1.3. Artefacts: Diagnostic Outcomes and Quality

Table 3-2 shows that artefacts occurred more frequently in studies with an indeterminate outcome compared to those that were conclusive. Motion or streak artefact, or both, were present in 80 % (N=24) of the 30 indeterminate studies, but in only 40 % (N= 79) of the 196 conclusive CTPA scans. The findings of this research mirror the literature as reviewed in section 1.2.2, in that motion artefact was by far the commonest artefact, followed by streak artefact. As outlined in 1.3.1, early work by Jones and Wittram (2005), using older 4 or 16 detector row scanners, found motion artefact to be the major image degrading factor in 74.3% of indeterminate studies.

In a recent study by Yeo et al (2017) motion artefact was, however, present in only 7 out of the 24 indeterminate studies compared to 19 out of 30 indeterminate studies identified in our research (Yeo, Zhou and Lim, 2017). It is therefore concerning that this research found a high incidence of motion artefact despite using modern scanners.

This may relate to patient factors such as dyspnoea, poor cooperation or incorrect breathing technique or instruction during scan acquisition. It is also possible that due to higher disease burden in a developing country, our patients are generally sicker than those in a First World setting, and less able to hold their breath during the scan.

4.1.4. Indeterminate Diagnostic Outcomes

As outlined in Section 1.3.1, adequate CTPA image quality remains key to allow confident radiological diagnosis or exclusion of pulmonary embolism. The mean rate of indeterminate studies is quoted in the literature as 6.4 %, with a range of 0.5 – 10.8%. Poor contrast opacification and motion artefact are still the main degrading factors, but as scanner speed advanced, contrast opacification surpassed motion artefact as the major factor impacting on CTPA image quality (Yeo, Zhou and Lim, 2017: 18-19), (Jones and Wittram, 2005:329).

Table 3-1 and Table 3-3 summarised the results relating to MPOT contrast opacification and diagnostic outcome in our study. The proportion of diagnostic scans was 86.7%, with 22% of studies positive for pulmonary embolism. The percentage of positive scans compared favourably with a similar study that found a positive rate of 20 % (Yeo, Zhou and Lim, 2017). In another study executed at three different hospitals, positive rates of between 14 and 49 % were obtained (Afzal, Colapinto and Haider, 2015).

Compared to the published literature, the percentage of diagnostically indeterminate studies was significantly higher in this study comprising 13.3 % (N=30) out of 226 CTPA scans reviewed. These were studies where the reporting radiologist could not confidently diagnose or rule out pulmonary embolism up to the segmental level. It appears that inadequate contrast opacification, a higher-than-expected incidence of artefacts, and possibly patient health risk factors and body habitus, influenced this result. Currently, validated clinical scoring systems such as the WELLS score is not universally applied to pre-select patients for CTPA studies at our institution. Lower pre-test probability has been shown in previous research to lead to more

indeterminate results, so this could also have influenced the number of indeterminate studies (Noschang *et al.*, 2018: 178-179).

4.1.5. Impact of Inadequate Contrast Opacification on diagnostic outcomes

Similar to the New Zealand study, contrast opacification was below threshold in 50 % of the indeterminate studies. However, artefacts occurred more frequently in our indeterminate group compared to theirs (80 % versus 30 %). As summarised in section 3.2.1, the findings of our research confirmed a statistically significant relationship between adequate MPOT contrast opacification and a conclusive scan outcome.

4.1.6. Health Risk Factors, Image Quality and Effective Dose

It is not known what the ratio between investigations for acute or chronic pulmonary emboli were in other studies, however, in this research the small group of patients investigated for chronic thrombo-embolism were statistically less likely to have motion artefact present. A possible explanation is relative clinical stability and less respiratory dyspnoea compared to the acute group.

It is not clear why patients with a history of surgery had statistically lower MPOT contrast opacification and increased streak artefact (Section 3.2.3).

As in the literature (Chen *et al.*, 2017; Yeo, Zhou and Lim, 2017) this research also identified increased body habitus as a contributing factor to suboptimal image quality. A relatively large proportion (42%) of patients in our research had shoulder measurements ≥ 35 cm and an even higher proportion in the indeterminate group (46%) fell into this category (Sections 3.1.2 and 3.2.3). It is unfortunately not possible to compare this figure with the literature, as no previous studies listed the exact proportion of smaller and larger patients, despite analysing the impact of larger patient size on image quality and dose.

Using Pearson's analysis, strong statistical correlations were found between shoulder measurement and contrast opacification, and shoulder measurement and effective dose (Section 3.2.3). These relationships were further confirmed by Chi-

square tests (Section 3.2.3). Larger patients had lower MPOT contrast opacification and required higher radiation doses. As the size of the patient increases, photon starvation artefact and increasing image noise becomes problematic, requiring compensatory increase in radiation dose. Apart from large body habitus, no other health risk factors were found to be statistically associated with effective dose.

4.1.7. Health Risk Factors and Diagnostic Outcomes

As surgery is a recognised risk factor for thromboembolic disease, it was surprising that in our study recent surgery statistically decreased the chance of a positive PE finding.

4.1.8. Diagnostic Findings and Clinical Outcomes

As expected in view of a potentially fatal diagnosis, mortality data at 1, 3 and 6 months indicate that patients with a positive diagnosis of PE had a higher mortality rate at all three endpoints, compared to patients with negative and indeterminate scans. There was no statistically significant association between indeterminate scan outcome or the MPOT contrast opacification HU value and mortality. This is interesting, as it is cautioned in the literature that nondiagnostic scans may impact adversely on patient management and mortality (Jones and Wittram, 2005). In our study, the majority of patients who demised within six months of scan date either had large pulmonary emboli or serious comorbid conditions such as sepsis or advanced malignancy.

It is, however, important to note that clinicians often regard indeterminate scans as ‘negative’, seldom asking for repeat or alternative imaging. Out of all the studies reviewed, only one repeat CTPA was subsequently performed, and three ventilation-perfusion scintigraphy scans. Where this information was available in this research, 80 % of indeterminate studies were regarded as negative by clinicians, compared to a range of 33 to 82% quoted in other studies (Yeo, Zhou and Lim, 2017: 22-23).

It is still recommended that indeterminate CTPA findings are discussed directly with referring clinicians, to make sure the implications are correctly understood and the

potential need for repeat imaging evaluated in the clinical context. Follow up imaging may also be recommended in the radiology report (Jones and Wittram, 2005).

Alternative or additional diagnostic CT findings were present in the majority (85 %) of studies, as illustrated in Table 3-3 and Figure 3-4. Therefore our findings agree with statements by other authors that CTPA studies add significant diagnostic value, even when negative or indeterminate for PE (Bělohlávek, Dytrych and Linhart, 2013: 135).

4.2. Limitations of the study

The study was conducted at a single academic/ tertiary level hospital – results may not be applicable to primary or secondary level institutions in the Western Cape or other provinces with a different demographic composition.

Due to departmental staff, budget and time constraints, measurements and observations were performed by a single reviewer (the author) in addition to the findings of the initial reporting radiologist. To improve accuracy, the mean of two measurements were used where applicable. Although the main variables of the study are objectively measurable, an element of subjectivity is inherent in interpretation and reporting of diagnostic imaging.

Currently radiology reporting for pulmonary embolism at Groote Schuur Hospital is done in traditional prose style and does not utilise a standardised template. Subjective assessment by different reporting radiologists of variable levels of experience may decrease reliability of findings stated in the reports.
As the research was conducted retrospectively, it was not possible to monitor certain aspects of CTPA protocol such as contrast administration and breathing manoeuvres in real time.

At our institution, clinical validation scores are not used uniformly to screen patients prior to CTPA studies being performed. In addition to image quality, factors relating to pre-test probability could also have influenced the diagnostic outcome of the scans, although investigation of this aspect was not within the scope of this research.

Mortality follow up data, although insightful, is incomplete as several patients were lost to follow up at 1, 3- or 6-month time intervals.

4.3. Recommendations and future research

Low contrast attenuation and respiratory motion artefacts were identified as major factors degrading image quality in this review. Optimisation of breath holding technique, and attention to the cannula size and rate of intravenous contrast administration may result in better MPOT contrast opacification, reduction of artefacts and higher rate of conclusive PE diagnoses. In particular, based on the findings of this and previous research, it should be considered to eliminate deep inspiration, and rather use only breath hold or expiratory phase CTPA technique. (Refer to section 1.3.1). This could already be implemented, and possibly further evaluated in future research.

In view of the high proportion of patients with large body habitus, future research evaluating the impact of individualising radiation dose settings for different sized patients may be undertaken, as in a US based image quality dose optimisation study (Chen *et al.*, 2017). A simple audit of CTPA dose could also be conducted.

It has been shown in the literature that a high pre-test probability increased diagnostic yield of CTPA scans. It was not a focus of this study, but future research could incorporate validated clinical scoring systems and assess the impact on diagnostic yield and study outcomes.

Lastly, in view of the current SARS-2-COV coronavirus pandemic, a repeat review investigating the image quality and/ or diagnostic yield of COVID-19 related CTPA studies may yield interesting comparative findings, as these patients tend to be particularly dyspnoeic during CTPA scans.

5. CONCLUSION

This is the first review of Computed Tomography Pulmonary Angiogram image quality at a major Western Cape Tertiary hospital, and to the author's knowledge in South Africa. In line with previous work by other authors worldwide, it was found that major factors degrading image quality were low contrast opacification and motion artefact. In this research, indeterminate outcomes often resulted from a combination of both suboptimal MPOT contrast attenuation and artefact.

Contrast opacification did meet the target threshold of ≥ 211 Hounsfield Units in > 90 percent of studies, which was favourable compared with published literature. The proportion of CTPA scans with indeterminate diagnostic outcomes was, however, almost double the mean rate quoted in the literature with a high incidence of motion artefact, and these aspects need optimisation. Patient related factors, such as a high percentage of patients with large body habitus, and the fact that the vast majority of scans were requested for suspected acute pulmonary embolism, may partially explain these findings.

Alternate or additional diagnostic CT findings were, however, present in the vast majority of cases. This added significant value and appeared to guide clinical decision making even when the scans were negative or indeterminate for a diagnosis of pulmonary embolism. Our study confirmed the known bias for clinicians to interpret indeterminate scans as negative, however, this had no significant impact on mortality.
Patients who demised within 6 months of the scan date were found to have either large pulmonary emboli, or significant co-morbid conditions such as advanced malignancy or sepsis.

Recommendations for future research and practice optimisation includes a focus on breath holding and contrast administration techniques, audit and optimisation of radiation dose, introducing and evaluating the impact of validated clinical scoring systems for CTPA requests and performing a similar review currently in the context of the SARS-2-COV pandemic.

6. REFERENCES

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7. APPENDICES

7.1. Appendix A: Ethical Approval

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: sumayah.arlefdien@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

19 August 2019

HREC REF: 520/2019

Dr S Moosa
Department of Radiation Oncology
Division Diagnostic Radiology
C-Floor, NGSH

Dear Dr Moosa

PROJECT TITLE: A RETROSPECTIVE REVIEW OF COMPUTED TOMOGRAPHY PULMONARY ANGIOGRAPHY IMAGE QUALITY AND THE IMPACT ON DIAGNOSTIC OUTCOME AT A TERTIARY SOUTH AFRICAN HOSPITAL (MMED CANDIDATE - DR J HOLTZHAUSEN)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 August 2020.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

We acknowledge that the student: - Dr Jeanette Holtzhausen will also be involved in this study.

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Institutional Review Board (IRB) number: IRB00001938
NHREC-registration number: REC-210208-007

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use: Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines. The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

7.2. Appendix B: HREC Annual Progress Report

HUMAN RESEARCH ETHICS COMMITTEE
19 AUG 2020
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

FHS017: Annual Progress Report / Renewal

Record Reviews/Audits/Collection of Biological Specimens/Repositories/Databases/Registries

HREC office use only (FWA00001637; IRB00001938)			
This serves as notification of annual approval, including any documentation described below.			
☑ Approved	Annual progress report	Approved until/next renewal date	30.08.21
☐ Not approved	See attached comments		
Signature Chairperson of the HREC/ Designee		Date Signed	21/8/2020

Please note that incomplete submissions will not be reviewed.
Please email this form and supporting documents (if applicable) in a combined pdf-file to

Please clarify your plan for research-related activities during COVID-19 lockdown

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	19 AUG 2020.		
HREC REF Number	520/2019	Current Ethics Approval was granted until	30 AUG 2020
Protocol title	A RETROSPECTIVE REVIEW OF COMPUTED TOMOGRAPHY ANGIOGRAPHY IMAGE QUALITY AND THE IMPACT ON DIAGNOSTIC OUTCOMES AT A TERTIARY SOUTH AFRICAN HOSPITAL (MMED - DR J. HOLTE/HAUSEN)		
Principal Investigator	DR S MOOSA		
Department / Office Internal Mail Address	Department of Radiation Oncology / Medicine. Division of Diagnostic Radiology C-Floor, NGSH.		
1.1 Does this protocol receive US Federal funding?		☐ Yes	☑ No

2. Protocol status (tick ✓)

☐	Research-related activities are ongoing
☑	Data collection is complete, data analysis only

Please indicate (in the block below) the titles and HREC reference numbers of any projects currently making use of the Database/registry/repository.

Only the M.Med project referenced above - HREC 520/2019

3. Protocol summary

Total number of records or specimens collected, reviewed or stored since the original approval		231
Total number of records or specimens collected, reviewed or stored since last progress report		N/A.
Have any research-related outputs (e.g. publications, abstracts, conference presentations) resulted from this research? If yes, please list and attach with this report.	☐ Yes	☑ No

4. Signature

Signature of PI		Date	18/08/2020

7.3. Appendix C: Hospital approval

Western Cape Government
Health

GROOTE SCHUUR HOSPITAL
Enquiries: Dr Bernadette Eick
e-mail: Bernadette.Eick@westerncape.gov.za

Dr Sulaiman Moosa
DIAGNOSTIC RADIOLOGY

E-mail: moosasulaiman@googlemail.com / a.esmail@uct.ac.za / Jeanette.Holtzhausen@gmail.com

Dear Dr Moosa,

RESEARCH PROJECT: A Retrospective Review Of Computed Tomography Pulmonary Angiography Image Quality And The Impact on Diagnostic Outcome At A Tertiary South African Hospital (MMed. Dr Jeanette Holtzhausen)

Your recent letter to the hospital refers.

You are granted permission to proceed with your research, which is valid until **30 August 2020.**

Please note the following:

a) Your research may not interfere with normal patient care.
b) Hospital staff may not be asked to assist with the research.
c) No additional costs to the hospital should be incurred i.e. Lab, consumables or stationary. **If access to TRACK Care/NHLS is required, kindly attach our letter of approval to the application form.**
d) **No patient folders may be removed from the premises or be inaccessible.**
e) Please provide the research assistant/field worker with a copy of this letter as verification of approval.
f) Confidentiality must always be maintained .
g) Should you at any time require photographs of your subjects, please obtain the necessary indemnity forms from our Public Relations Office (E45 OMB or ext. 2187/2188).
h) Should you require additional research time beyond the stipulated expiry date, please apply for an extension.
i) Please discuss the study with the HOD before commencing.
j) Please introduce yourself to the person in charge of an area before commencing.
k) On completion of your research, please forward any recommendations/findings that can be beneficial to use to take further action that may inform redevelopment of future policy / review guidelines.
l) Kindly submit a copy of the publication or report to this office on completion of the research.
m) At no time should any posters encouraging patients to partake in research, be displayed within a clinical area.

I would like to wish you every success with the project.

Yours sincerely

DR BERNADETTE EICK
CHIEF OPERATIONAL OFFICER
Date: 25 September 2019

C.C. Mr. L. Naidoo
Dr H. Aziz
Professor S. Beningfield

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7.4. Appendix D: Renewal of Hospital approval

Western Cape Government
Health

GROOTE SCHUUR HOSPITAL
Enquiries: Dr Bernadette Eick
E-mail : *Bernadette.Eick@westerncape.gov.za*

Dr Sulaiman Moosa
DIAGNOSTIC RADIOLOGY

E-mail: moosasulaiman@googlemail.com / Jeanette.Holtzhausen@gmail.com

Dear Dr Moosa,

RESEARCH PROJECT EXTENSION: A Retrospective Review of Computed Tomography Pulmonary Angiography Image Quality And The Impact On Diagnostic Outcome At A Tertiary South African Hospital (MMed. Dr Jeanette Holtzhausen)

Your recent communication to the hospital refers.

The extension of your research is approved in accordance with UCT Ethics clearance, until **30 August 2021**.

As previously mentioned,

a) Your research may not interfere with normal patient care.
b) Hospital staff may not be asked to assist with the research.
c) No additional costs to the hospital should be incurred as indicated in your Annexure 2 i.e. Lab, consumables or stationery. **If access to TRACK Care/NHLS is required, kindly attach our letter of approval to the application form and approach Information Management to assist with data.**
d) **No patient folders may be removed from the premises or be inaccessible.**
e) Please provide the research assistant/field worker with a copy of this letter as verification of approval.
f) Confidentiality must always be maintained.
g) Once the research is complete, please submit a copy of the publication or report.

I would like to wish you every success with the project.

Yours sincerely

DR BERNADETTE EICK
CHIEF OPERATIONAL OFFICER
Date: 14 October 2020

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