The Relation Between Elevated D-dimer Levels and a Positive Computed Tomography Pulmonary Angiogram to Confirm Pulmonary Emboli: A Retrospective Study

by

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A dissertation submitted in the fulfilment of the requirement for the degree

MAGISTER OF RADIOGRAPHY

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Declaration

I, Rochelle Antoinette Kruger, declare that this dissertation, entitled 'The Relation Between Elevated D-dimer Levels and a Positive Computed Tomography Pulmonary Angiogram to Confirm Pulmonary Emboli: A Retrospective Study', is a presentation of my own original research work conducted at the Central University of Technology, Free State. Wherever contributions of others were involved, every effort has been made to indicate this clearly, with due reference to the literature and acknowledgement of collaborative research and discussions. No part of this dissertation has been submitted for any other degree or professional qualification.

Rochelle A. Kruger

July 2023

I certify that the above statement is correct.

Supervisor Dr Henra Muller

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Dedication

This work is dedicated to The Most High, my Heavenly Father. None of this would have been possible without His favour, strength, and authority. Thank You, Lord, for saving, guarding, and protecting me through this season in my life.

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My reflection

"Caring for people produces lasting relationships that enable people to live a better life."

Rochelle Kruger

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Abbreviations

ACR:	American College of Radiology
ALARA:	As low as reasonably achievable
cm:	Centimetres
CM:	Contrast media
COVID-19:	Coronavirus disease 2019
CT:	Computed Tomography
CTDI:	Computed Tomography Dose Index
CTPA:	Computed tomography pulmonary angiography
DCI:	Data capturing instrument
DD+:	D-dimer positive
DD-:	D-dimer negative
DLP:	Dose-length product
DRL:	Diagnostic reference level
DVT:	Deep vein thrombosis
HSREC:	Health Sciences Research Ethics Committee
ICRP:	International Commission of Radiation Protection
kg:	Kilogram
kVp:	Kilo voltage peak
mA:	Milliampere
mAs:	Milliampere per second
MDCT:	Multidetector Computed Tomography
mg:	Milligrams
mg/ml:	Milligrams per Millilitre

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mGy:	Milligray
mGy/cm:	Milligray centimetre
mg/l:	Milligram per Litre
ml:	Millilitre
mm:	Millimetre
MRI:	Magnetic resonance imaging
mSv:	Millisieverts
ng:	Nanogram
ng/ml	Nanogram per millilitres
NPV	Negative predictive value
NR:	Non-reported chest pain
PE:	Pulmonary embolism
PACS:	Picture Archiving and Communication System
SARS-CoV-19	Severe Respiratory Syndrome Coronavirus 2019
Tc-99	Technetium-99m
VCT:	Volumetric Computed Tomography
V/Q:	Ventilation-perfusion lung scintigraphy

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Glossary

Bolus tracking technique: "Bolus tracking represents the most widespread method for timing the scan start of CT angiography with the injection of contrast media. The technique monitors the contrast enhancement in a user-defined vessel and after a threshold is reached, the scan is initiated after a predefined and fixed trigger delay" (Hinzpeter et al., 2019).

Computed Tomography Pulmonary Angiography: "Diagnostic imaging modality for diagnosing pulmonary emboli using radiation exposure and iodinated contrast medium. This technique is excellent for including and excluding pulmonary embolisms and has become the first-choice diagnostic imaging technique" (Doğan et al., 2015).

Computed Tomography: "Computed tomography is a multidetector radiographic scanning technique for three-dimensional human body imaging. "Radiologic imaging studies have become an integral diagnostic tool in the practice of clinical medicine" (Parker et al., 2005).

D-dimer: "D-dimer is a protein product of cross-linked fibrin degradation that is present in the blood of healthy individuals in a negligible amount (of the order 100–200 ng/ml). The evidence of increased fibrinolysis and elevated blood concentration of D-dimer indicates intravascular coagulation and thrombotic disease" (Lippi et al., 2014).

D-dimer tests: "An established clinical laboratory test used routinely to assess patients suspected of suffering a pulmonary embolism, deep vein thrombosis and venous thromboembolism. The D-dimer test has become established to assess patients suspected of suffering pulmonary embolism" (Van der Hulle et al., 2016).

Deep Venous Thrombosis: "A blood clot in a deep vein, usually in the legs. This condition is serious because blood clots can loosen and lodge into the lungs" (Mayo Clinic, 2021: online).

Pulmonary Embolism: "A lodgement of a clot resulting in obstruction in a pulmonary artery, with subsequent obstruction of the blood supply to the lung parenchyma. The peripheral pulmonary artery may be partially or completely occluded, resulting in pulmonary infarction with pleuritic pain"" (Hui et al., 2018).

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Abstract

Introduction: Pulmonary embolism (PE) is one of the most common heart and blood vessel diseases in the world, and can have life-threatening complications. Acute PE is a leading cause of hemodynamic instability and mortality and is the third most common cardiovascular condition after coronary artery disease and stroke. Therefore, timeous diagnosis and proper treatment of PE are imperative to manage this life-threatening condition. PE is diagnosed using laboratory tests and imaging procedures, of which computed tomography pulmonary angiography (CTPA) is the 'gold standard'. One of the most important laboratory tests is the assessment of D-dimer levels in the blood. Patients with elevated D-dimer levels are routinely referred for CTPA to rule out PE; however, PE is not always confirmed in these referred patients. Consequently, growing evidence suggests overuse of CTPA, which increases the risk of radiation dose and adverse effects from contrast media administration.

Aim: This retrospective South African study was conducted in a single private radiology practice in Bloemfontein to determine the relation between an elevated D-dimer level and a positive CTPA, using the picture archiving and communication system (PACS) of patient information.

Methods: The data of 1 219 patients, which included 158 COVID-19 referrals, were recorded using a predesigned data capturing instrument. The data variables included biographical information, clinical indicators, and imaging condition values.

Results: Overall, the number of patients in the sample population (n = 1 219) with a positive diagnosis of PE was relatively small, at only 16.7%. Of these patients, approximately 50% had elevated D-dimer levels, which was also true for the subpopulation excluding COVID-19 referral patients. In contrast, a few patients (less than 20%) of the subgroup with elevated D-dimer levels had a positive diagnosis of PE. These results show that, although approximately half the patients

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diagnosed with PE had elevated D-dimer levels, only a few patients with elevated D-dimer levels were diagnosed with PE. This necessitates further investigation into the required routine best practices when deciding which patients should be referred for CTPA during the routine PE workup. In particular, clinical decision rules for PE need refining, especially to limit unnecessary CTPA referrals.

Conclusion: The findings of this study may result in the revision of PE workups in the private practice and also assist with the development of practice guidelines to ultimately improve the quality of service.

Keywords: pulmonary embolism, D-Dimer levels, computed tomography pulmonary angiography, diagnosis, radiation dose, contrast medium, COVID-19, picture archiving and communication system, data capturing instrument

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Chapter 1

Introduction to the Study

1.1 Background to the research project

Although computed tomography pulmonary angiography (CTPA) is the method of choice for the diagnoses of pulmonary embolism (PE), the rate of indeterminate studies is estimated as 6,6%. The second most common cause of indeterminate CTPA testing is ovation, due to insufficient contrast enhancement. Accurate diagnoses of PE are imperative, because, if untreated it involves high morbidity and mortality. PE occurs when a blood clot embolises the lungs from peripheral veins and causes an occlusion of the blood supply to a portion of the lung. This prevents oxygenated blood from reaching the brain and other vital organs. The exact prevalence of PE in South Africa in unknown. However, in 2016, 2 124 deaths were reported from pulmonary vascular diseases, including PE (Basson & Moodley, 2022).

In most patients, the natural course of acute PE is complete fibrinolysis, with almost complete resolution of vascular occlusion, decreased pulmonary vascular resistance, and restoration of normal hemodynamics (Davies-van Es et al., 2023). A high incidence of thromboembolic pneumonia and venous thromboembolism has been commonly reported in patients with COVID- 2019 infection. Venous thromboembolism, especially pulmonary embolism, can have devastating consequences if left untreated. The hypercoagulable state of patients with SARS-CoV-2 pneumonia increases the risk of developing PE. Pulmonary emboli commonly occur in patients with underlying cardiovascular abnormalities, those with advanced age, in bed-bound patients, patients with high body mass index and those with postoperative complications (Ahlers & Said-Hartley, 2022).

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Pulmonary embolism one of the most common heart and blood vessel diseases in the world, with life-threatening complications. It is the third leading cause of cardiovascular mortality in the United States of America (Osho & Dudzinski, 2022). It is estimated that 200 000 to 500 000 patients are diagnosed with PE annually in the United States of America (Keizer Permanente Washington, 2022). PE occurs when a blood clot dislodges from the systemic venous system and blocks an artery in the lungs, which could cause shortness of breath and chest pain, particularly when breathing in and coughing up blood. In addition, it may cause total or partial occlusion, resulting in dysfunctional pulmonary circulation and changes in lung parenchyma and the respiratory system. In acute cases, PE may be fatal (Al-Rammah et al., 2016).

Acute PE is one of the leading causes of hemodynamic instability and mortality. It is the third most common cardiovascular condition after coronary artery disease and stroke (Moore et al., 2018). Therefore, the timeous diagnosis and treatment of PE are imperative to manage this life-threatening condition. Diagnosing PE involves laboratory tests and imaging procedures. One of the important diagnostic laboratory tests is determining the D-dimer levels in the blood. Routinely, patients may also receive a chest X-ray to evaluate their lungs, an ultrasound of the lower limbs to eliminate possible deep vein thrombosis (DVT) and, possibly, a computed tomography pulmonary angiogram (CTPA) to confirm PE (Youssf et al., 2014).

D-dimer testing is usually the first routine assessment for patients with suspected PE, although other tests, such as nuclear planar ventilation-perfusion (V/Q) imaging, and echocardiogram, can also be performed to determine the presence of PE. A D-dimer laboratory test measures the protein products of cross-linked fibrin (D-dimer) present in the blood (Lippi et al., 2014). In healthy individuals, the normal negligible amount of D-dimer varies between 100 and 200 ng/ml. A D-dimer test value of <500 ng/ml is regarded as a negative test, which is indicative of a low probability of PE.

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On the other hand, D-dimer levels >1 000 ng/ml are indicative of an increased probability of PE, which may produce severe embolitic obstruction (Tick et al., 2008).

Moreover, PE is a life-threatening condition might lead to the dysfunction of the heart's right side. According to Youssf et al. (2014), accuracy and rapid diagnosis of PE remain difficult in clinical practice, because of its non-specific clinical presentation. Objective testing is required to establish or exclude the presence of PE. Therefore, early diagnosis is of the utmost importance to detect PE. According to Youssf et al. (2014), CTPA is considered the gold standard diagnostic technique to demonstrate PE in patients with elevated D-dimer levels.

Currently, CTPA is the diagnostic imaging 'gold standard' for PE. Computed tomography (CT) imaging provides a highly accurate representation of a patient's anatomy, is not invasive and is widely available (Youssf et al., 2014; Ahmed et al., 2022). CTPA also has a high specificity and sensitivity for PE (Pathak et al., 2011; Doğan et al., 2015). These advantages of CT have led to increased requests for CTPA examinations to confirm PE (Sun & Lei, 2017). Consequently, hospitals and private radiology practices perform CTPA examinations on patients with suspected PE daily.

Diagnostic imaging procedures, especially CTPA, carry the risk of high radiation exposure for patients referred for PE diagnosis. With the increased uptake of and access to CT imaging, care should be taken when exposing a patient to ionising radiation, because it may have stochastic and/or deterministic effects (Brenner & Hall, 2007). An image-enhancing contrast medium (CM) administration during CTPA is also required to diagnose PE accurately. CM administration into the human body may produce an allergic reaction of various forms, such as anaphylactic shock, skin reaction (swelling and redness), nausea, metal taste in the mouth, and possible renal impairment in the future (Naufal, 2012).

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The worldwide viral pandemic of COVID-19 reached the shores of the African continent in February 2020. COVID-19 is a highly contagious transmissible virus that has high morbidity, resulting in the rapid which can be potentially fatal disease. The clinical presentation of the COVID-19 viral infection is associated with severe respiratory systemic inflammation, which gives rise to fatigue, dyspnoea, coughing, fever, hypoxia, myo-arthralgias, anoxia, elevated D-dimer levels, and loss of taste (Li et al., 2020). Due to an increase in COVID-19 infections in the Free State province, CTPA requests at the radiology practice increased. CTPA scans were performed on all patients who had tested positive for COVID-19 and who presented with increased D-dimer levels and chest pain.

A study conducted in a tertiary academic hospital setting in South Africa involved 63 retrospective patients and 149 prospective patients with PE who received CTPA (Basson & Moodley, 2022). In total 19 CTPAs were excluded from the prospective review due to incomplete informed consent. Insufficient contrast enhancement was found in 19% (12/63) of retrospective cases and 20.8% (27/130) of the prospective cases. The high rate of inadequate contrast-enhanced studies might significantly impact the institution's accurate diagnosis of PE (Basson & Moodley, 2022).

Diagnoses of PE were confirmed in 37 cases (37%) in a study conducted at Charlotte Maxeke Hospital in South Africa. This yield rate, corresponded with several studies performed elsewhere, where yield rates were in the range of 9%—16%. Even when compared to the PIOPED study, which had a higher yield rate, of 23% (n = 15), the study compared positively. This comparison may relate to a better clinical assessment rate, and a lack of D-dimer values and Wells scores on referral letters merely a sign of a documentation omission, indicating that the clinical decision rule was not followed. Therefore, the high yield rate may be due to other reasons, which warrant further considerations (Dorfman, 2016).

The radiological procedure of CTPA is a particular area of interest to the researcher. CTPA is the radiological examination used to diagnose PE at the private practice where the researcher is employed. During daily practice, the researcher observed that clinicians referred many patients with

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positive D-dimer tests and chest pain for CTPA to this specific practice. Data from this private practice's picture archiving and communication system (PACS) indicated that 551 CTPA examinations were executed in 2017, 580 in 2018, 666 in 2019 and 813 in 2020 and 355 in 2021. Also noteworthy is that clinician referrals lacked information, particularly about clinical decision rules and previous imaging. The lack of information gave rise to numerous questions associated with the increased requests for CTPA examinations to diagnose the presence or absence of PE (PACS, accessed 13 February 2021).

1.2 Problem statement

In a private radiology practice in Bloemfontein, Free State, South Africa, where the researcher was employed at the time of the study, CTPA was the primary imaging method used to diagnose PE. In this practice, clinicians referred many patients with positive D-dimer tests and chest pain for CTPA. Before the COVID-19 pandemic, the number of patients referred for CTPA was in the order of 600 per annum. In the first year of the pandemic, 2020, the number of patients referred for CTPA increased to 813. In the second year of the pandemic, the number of CTPA patients more than doubled to 1 968. Many COVID-19 patients who visited this practice demonstrated elevated D-dimer levels and chest pain and were, consequently, referred for CTPA to ascertain if PE was also present. The researcher ascertained before the study that numerous patients with elevated D-dimer levels who had been scheduled for a CTPA did not have PE, this observation led to the execution of the study. The research question that emerged was: How effective was the execution of CTPA, and was it justified to confirm PE in patients with elevated D-dimer tests, chest pain and suspected PE?

Subsidiary question: What is the relation between an elevated D-dimer test and a CTPA demonstrating PE, according to a retrospective research study? Additional/subsidiary questions to be answered are:

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1) Does the radiation dose that a patient receives when undergoing a CTPA justify this diagnostic test for all patients with a positive D-dimer test and acute chest pain?
2) Does iodinated CM administration in CTPA increase the patient's risk of future adverse effects on their kidney function and pose a risk for an allergic reaction?

1.3 Research statement

The execution of CTPA for all patients with an elevated D-dimer test and chest pain was not justified to confirm PE.

1.4 Aim and objectives

The aim of the study was to establish if there is a relationship between an elevated D-dimer level and a positive CTPA, which confirms the presence of PE, for all patients with chest pain and suspected PE. The observation that many patients with elevated D-dimer levels who had been scheduled for a CTPA did not have PE means that if the referral for CTPA had been based solely on increased D-dimer levels, the patients had been exposed to a seemingly unjustified radiation dose and CM administration. The question arose: what is the relation between elevated D-dimer levels and the confirmation of PE through CTPA? This knowledge would be advantageous in the clinical workup of patients in this practice. At this practice, patients' clinical information is stored on the picture archiving and communication system (PACS); therefore, a retrospective study was undertaken to determine the relation between an elevated D-dimer level and a positive CTPA to confirm PE, using the PACS patient information.

To meet the aim of the study, the following objectives were devised:

1. To design a novel data capturing instrument (DCI) for data related to elevated D-dimer levels and a positive PE diagnosis following CTPA (*based on review of literature and PACS data categories);

2. To evaluate the suitability of the newly designed DCI (*using focus group discussion with CT experts and pilot study); and

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3. To determine the relation between elevated D-dimer levels and positive PE diagnosis following CTPA (*this would be achieved through data analysis).

1.5 Summary of methods

Research methodology refers to the scientific accumulation and acceptance of knowledge that has been formulated systematically, and which references supporting general operational laws (practice CTPA protocols and contrast media (CM) protocol). Knowledge is also obtained by applying scientific methods (De Vos et al., 2002). For this retrospective study, a quantitative, descriptive study design was used to examine the characteristics of a sample of patients. Uys and Basson (2005:38) posit that a descriptive study design describes a situation accurately and carefully while it accumulates data in the original environment. Polit et al. (2001) postulate that a quantitative approach enables the researcher to analyse data using numerical information and statistical procedures.

A research design is regarded as a blueprint for conducting a study that enhances control over external factors that could interfere with the validity of the study results. The probability that the study results are accurate reflections of realities is increased by the control provided by design (Polit & Beck, 2008; Burns & Grove, 2005). Some researchers consider a research design to be the entire strategy for a study, from problem identification to the final data collection plans. Other researchers limit the design to clearly defined structures within which the study is implemented (Burns & Grove, 2005; Uys & Basson, 2005).

The study population included all patients referred for CTPA examination from 1 January 2019 to 31 December 2020 at the radiology practice in Bloemfontein where the investigation was conducted. The researcher conducted a pilot study using a checklist to identify possible flaws or assess time requirements (Polit & Beck, 2008). Once ethical approval from the Health Sciences Research Ethics Committee (HSREC) of the University of the Free State had been received, the researcher randomly selected a sample size of 10 patients from the patients who had undergone CTPA examinations in a year from the PACS database. The data collection sheet required no major corrections or adjustments. The data collected during the pilot study were also included in the study.

The research project was conducted in a private diagnostic radiology practice in Bloemfontein, in the Free State province of South Africa. The data of 1 219 patients, recorded on the PACS, were used

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to determine the relation between an elevated D-dimer level and a positive PE. To record the data on the PACS, a data-capturing instrument (DCI) was designed and then tested so that it could accurately (valid) and consistently (reliable) capture patient data on the PACS. After capturing the patient data with the DCI, the data of the variables were captured on Excel spreadsheets. The data variables included biographical information, clinical indicators, and imaging condition values. Summary statistics – means, percentages, and ranges – were calculated for the variables. Shapiro-Wilk tests were performed to determine whether the population data of the variables were normally distributed. Chi-square tests of independence were performed to ascertain if a relation existed between elevated D-Dimer levels in the blood and a positive PE diagnosis after CTPA.

1.6 Ethical considerations

Ethical approval for this study was granted by the University of the Free State HSREC, with ethical approval number UFS-HSD 2021/12809 (Appendix A). In addition, written permission to conduct the research study was obtained from the practice manager of the participating private radiology practice in Bloemfontein (Appendix B). Patient consent was not required for this study, because all data were gathered from the PACS database system of the participating private radiology practice. After extracting the patient data from the PACS database system, the data were anonymised to ensure patient privacy and confidentiality. The patient data used in the study are stored in a password-protected computer and will be kept for three years as prescribed by international research guidelines, after which it will be deleted.

The research process was guided by three fundamental ethical principles: respect for persons, beneficence, justice and integrity. These principles are based on human rights that must be protected in research: the right to fair selection and treatment, privacy and confidentiality, protection from harm, and informed consent (Brink, 2006).

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1.7 Significance of the research project

Knowledge of the relation between an elevated D-dimer and a positive PE diagnosis could be of value at this research site and could help to the change or assist with the routine workup of patients with suspected PE. Furthermore, knowledge could be a CTPA tool to achieve accurate outcomes for positive PE diagnoses at other facilities. Consequently, minimising the use of CTPA, which is a costly procedure (Appendix C) for patients with elevated D-dimer levels at the participating private radiology practice, will influence the clinical workup further, thereby reducing the number of patients exposed to radiation associated with CTPA. In addition, the outcome of this study may be used to plan in-service training for CT radiographers at the participating private radiology practice.

1.8 Limitations of the research project

This retrospective research project was limited to a single private radiology practice in Bloemfontein. The sample population was limited to patients for whom data were available on the PACS at the radiology practice. Furthermore, the data of some of the patients in this study who had been referred to the practice during the COVID-19 pandemic were incomplete. For example, not all patient records included patient referral letters, information on the amount of CM used, radiation dose, and whether a combination of CTPA and CT abdominal examinations was used. In terms of D-dimer levels, threshold values were not recorded, and specific D-dimer levels were absent on some referral letters. At the participating private radiology practice, the expertise and experience of the reporting radiologist could have brought about interobserver variability between reports. This variability hampers the generalisability of the results to other radiology departments.

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1.9 Layout of the dissertation

This dissertation is arranged into six chapters. Briefly, each chapter comprises the following content:

Chapter 1: Introduction to the study

In this chapter, the field of study was introduced, the research problem was identified, and the aim, significance, and limitations of the study, as well as a summary of the methodology, were briefly described.

Chapter 2: Literature review

In this chapter, the currently available literature on topics such as the causes, signs and symptoms of PE, the imaging of PE through CTPA, associated radiation dose, CM and its adverse effects, alternative tests to confirm PE, D-dimer testing, and coronavirus disease, will be discussed.

Chapter 3: Study design, materials and methods

In this chapter, the study design and methods used in this study will be discussed.

Chapter 4: Data capturing instrument

In this chapter, the study design instrument will be presented.

Chapter 5: Relation between D-dimer and PE confirmation with CTPA

In this chapter, the results of the relation between D-dimer and positive PE will be presented for the sample population, the subpopulation excluding COVID-19 referrals, and patients with a prehistory of PE, the subpopulation of patients with a

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prehistory of PE, and the subpopulation of COVID-19 referral patients. Furthermore, ancillary clinical findings during CTPA will be presented.

Chapter 6: Discussion and concluding remarks

In the final chapter, the key findings of this research project will be discussed and related to current understandings. This chapter will also provide concluding remarks on the study and recommendations for future research.

1.10 Funding

This postgraduate research study was funded by a research grant and scholarship from the Central University of Technology, Free State. The grant funded the tuition fees for two years, and project expenses.

1.11 Appendices

Appendix A: Ethical approval letter HSREC

Appendix B: Permission to conduct research study at the radiology practice

Appendix C: Cost of CTPA examination

Appendix D: Data capturing instrument

Appendix E: General Electric Light Speed quality assurance certificate

Appendix F: Department of Health Inspection Body: Certificate of Conformance

Appendix G: Department of Health Acceptance test and routine test lists

Appendix H: Quality control tomography tests

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Appendix I: Letter from the Biostatistician

Appendix J: Letter from the language editor

Appendix K: Turnitin report

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Chapter 2

Literature Review

2.1 Introduction

The vascular disease of pulmonary embolism (PE) is a serious condition that occurs when a blood clot forms in a lung artery. This condition, also called venous thromboembolic disease, is a life-threatening medical emergency requiring quick intervention and treatment (Al-Rammah et al., 2016). It is the third leading cause of cardiovascular death in the United States of America (Osho & Dudzinski, 2022). It is estimated that PE is responsible for the hospitalisation of more than 250 000 patients every year in the United States of America, and 10–30% of patients die within the first month after diagnosis (Moore et al., 2018). PE can be deadly, causing death in 22% of cases that were not diagnosed before causing death (Al-Rammah et al., 2016). In addition, PE presents symptoms resembling that of many other medical conditions, including heart attack and pneumonia, making it difficult to diagnose. Because of this potentially deadly situation, an accurate and swift diagnosis is required for appropriate treatment. As a result, several diagnostic procedures have been developed to support this medical emergency. One such procedure that plays a leading role in the workup of PE patients is computed tomography pulmonary angiography (CTPA). This diagnostic imaging procedure has a sensitivity of 83% and a specificity of as high as 96% in patients with suspected acute PE (Kubak et al., 2016).

2.2 Pulmonary embolism

The presentation of PE may be varied and clinically misleading. Clinical pulmonary symptoms depend on lung involvement, clot size, and underlying lung or heart disease (Morrone & Morrone, 2018).

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Common signs of PE include shortness of breath, chest pain and cough. Patients may also present with fever, rapid or irregular heartbeat, light-headedness, dizziness, leg swelling, pain, cyanosis, and excessive sweat. The clinical manifestation of PE usually presents with symptoms such as dyspnoea and pleuritic chest pain due to pulmonary infarction, leading to irritation of the pleura (Srivali et al., 2012). In some cases, the chest pain is non-specific, and haemoptysis may occur. Patients may also present with chest pain radiating to the arm, and PE is associated with lower limb or muscle swelling. Furthermore, patients might be asymptomatic, and sudden death may be the first presentation of the disease (Moore et al., 2018). Acute PE presents clinically with chest pain, hypotension, dyspnoea, cough, tachycardia, and haemoptysis. Cardiac arrest, shock, hypotension, and electrocardiography changes indicate severe PE. Lower extremity pain, oedema erythema, and deep vein thrombosis (DVT) might also be present (Moore et al., 2018).

Older people are disproportionately affected by PE. The incidence of PE in people over 70 years is three times greater than those aged 45 to 69 years (Turetz et al., 2018). Incidence in people aged 45–69 years is also three times greater than for people aged 20–44. This age-related increase in PE can be attributed mostly to the increase in PE burden (Meyer et al., 2010). The study by Turetz et al. (2018) indicates that the incidence of PE is higher in male patients than in female patients.

The mechanism of PE occurs through several means. Besides blood clots, occlusion in the blood vessels can result from air bubbles, a piece of a tumour, and fat from the bone marrow of fractured bones (Batalis & Harley, 2013). PE develops from the dislodgement of a deep-vein thrombus, most commonly from the lower limbs, which then 'embolises' to the arterial lung circulation, where it lodges and causes a partial or complete obstruction (Farag et al., 2022). The most common mechanisms for PE are traumatic injury or non-traumatic mechanisms, including the postoperative formation of blood clots, long periods of immobility, and health conditions such as heart disease, cancer, and other inflammatory diseases, for example, atherosclerosis and COVID-19. Lengthy car or plane trips could

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also cause PE by limiting the blood supply to the lower limbs and causing clot formation. These mechanisms increase the risk of blood or fat emboli and could cause pulmonary artery occlusion (Turetz et al., 2018).

2.3 Diagnosis of PE

The absence of defining symptoms makes the diagnosis of PE difficult. Therefore, diagnosis relies strongly on non-invasive imaging techniques. It is important to exclude PE, because of bleeding risks of anticoagulation and the costs associated with treatment and monitoring (Patel et al., 2020). Historically, nuclear planar ventilation-perfusion (V/Q) imaging and pulmonary angiography were used to demonstrate PE (Doğan et al., 2015). Both these methods have complications. V/Q imaging requires right heart catheterisation, and PE detection rates range from 45% to 66%. Until 1990, V/Q imaging was the imaging procedure of choice. However, this imaging modality has mostly been replaced by CTPA – a widely available, fast, and non-invasive imaging technique (Moore et al., 2018).

Several imaging techniques are used to evaluate PE. The primary methods include chest radiographs, V/Q imaging, computed tomography venography (CTV), and CTPA. Other methods are magnetic resonance imaging (MRI), magnetic resonance imaging pulmonary angiography (MRIPA), venous ultrasonography, echocardiography, and catheter pulmonary angiography (Moore et al., 2018). Although chest radiographs are not useful for diagnosing PE, they might reveal other pathologies, such as pneumonia, pulmonary oedema, and pneumothorax, in patients with acute chest pain. Although CTPA is preferred for PE diagnoses, V/Q imaging is still used in specific clinical situations. For instance, V/Q is used mainly in renal failure patients, young female patients, patients with an outsized body stature, pregnant females, and patients with contrast medium (CM) allergies. A V/Q scan has a 50-fold lower radiation dose to the breast tissue – 50–80 millisieverts (mSv) – with a 64-slice CT scanner (Moore et al., 2018). The ventilation agents most used in V/Q imaging are aerosolised

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Technetium-99m (Tc-99) labelled agent and diethylenetriaminepentaacetic acid (DTPA), which enables the facilitation of regional comparison for ventilation and perfusion sequences in multiple views (Moore et al., 2018). Before the scan is performed, the patient is administered an intravenous injection containing 200 000–700 000 particles of Tc-99 labelled macro-aggregated albumin (MAA). This scan is performed with the patient upright, thereby producing multiple planar images. This low-dose CT technique uses single-photon emission CTV scans that can be performed before or after perfusion and are interpreted in correlation with the most recent chest image taken within the previous 24 hours (Moore et al., 2018).

2.3.1 Scoring risk factors for diagnosis of PE

Determining the risk of PE in a patient is important for the purposes of planning diagnostic procedures. Clinical risk can be determined by applying stratified scoring methods, such as Wells (Wells et al., 2001) and Geneva (Wolf et al., 2004). The Wells score entails the application of a seven-point scoring system, where malignancy scores 1 point, haemoptysis 1 point, history of PE or DVT 1.5 points, tachycardia (>100) 1.5 points, and immobilisation (≥3 days) or recent surgery (within four weeks). According to Wells et al. (2001), if ≥ 1.5 points were allocated, that is likely to indicate that the patient will have a positive diagnosis of PE. Furthermore, Wells et al. (2001) awards 3 points for clinical signs and symptoms of DVT. The Geneva score is a three-level scoring system, where 0–1 indicates low risk, 2–6 indicates moderate risk, and >6 indicates high risk. A two-level approach (≤4 PE unlikely; >4 PE likely) recommends performing a D-dimer test on patients deemed 'PE unlikely' and a CTPA for patients deemed 'PE likely' (Van Belle et al., 2006). A D-dimer test is an assay for a plasmin-derived degradation product, which has a high sensitivity and negative predictive value for diagnosing venous thromboembolic disease (Schrecengost et al., 2003). However, if the D-dimer test is positive, patients should undergo CTPA for further evaluation (Van Belle et al., 2006). For patients older than 50, the D-dimer threshold value should be adjusted by

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multiplying age by 10. It is important to note that patients with sepsis, malignancy, pregnancy, myocardial infarction, or recent surgery may produce false positive D-dimer tests (Righini et al., 2014; Wang et al., 2020).

2.4 CTPA for PE imaging

Diagnosis of PE relies heavily on radiological imaging. In the early nineties, fast-speed helical CT scanners were introduced for vascular imaging and the diagnosis of PE. These multidetector CT (MDCT) scanners produces three-dimensional images and apply the technique of isotropic voxel imaging, and reduces the vascular invasiveness of conventional angiographic procedures (Moore et al., 2018). Using MDCT scanning provides a high level of image quality, resulting in an increased diagnostic performance compared to conventional pulmonary angiography, with a sensitivity varying between 83 and 100% and specificity between 89 and 96% (Moore et al., 2018). The 32, 64 and 128-slice CT scanners that are globally used for CTPA provide diagnostic performances equal to or surpassing conventional pulmonary angiography. In radiological practice, MDCT scanners have mostly replaced invasive pulmonary angiography by offering similar specificity and sensitivity for identifying PE in small pulmonary arteries, with reduced radiation dose (Sauter et al., 2016). This high specificity and sensitivity increase the possibility of identifying PE in small pulmonary arteries. Because of the non-invasive imaging nature of CTPA, it has become the method of choice for diagnosing PE (Doğan et al., 2015). The excellence and simplicity of CTPA as a diagnostic technique for PE have led to its increased use worldwide. Because of the relatively high radiation dose that patients receive with CTPA, the correct implementation of clinical decision rules in the workup for PE improves the proper use of CT (Pathak et al., 2011; Doğan et al., 2015). Although CTPA is considered the 'gold standard' imaging technique for PE diagnoses, it is costly, invasive, and not universally available (Youssf et al., 2014; Zantonelli et al., 2022).

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2.4.1 Radiation exposure with CTPA

In CTPA, three-dimensional images are produced by exposing a patient to radiation. For a CTPA examination, the entire thorax, from the lung apices to the diaphragm, including the upper part of the abdomen, is included in a craniocaudal direction for each patient. The CT scanners produce quality imaging by applying specific measures to reduce patients' radiation dose while still producing scans of diagnostic quality (Doğan et al., 2015). Despite CTPA being an excellent tool for diagnosing PE, risks of possible adverse effects of radiation exposure and administering intravenous CM remain challenging (Alshumrani et al., 2021).

The radiation through CTPA poses a risk to the sensitive organs of a patient undergoing a CT scan to diagnose PE, particularly the thyroid and breast. Hence, increased requests for CTPA have raised concerns about radiation exposure to these radiation-sensitive organs (Genena & Mohamed Selim, 2016). Studies have shown that CTPA delivers a much higher radiation dose than single X-ray exposure. For example, Genena and Mohamed Selim (2016) report that the CT image acquisition process requires 800–1 400 X-ray exposures around the patient, compared to a single X-ray exposure for a single image. Therefore, CTPA patients receive 100–400 times more radiation than from a single X-ray exposure. Therefore, CTPA protocols must comply with the 'as low as reasonably achievable' (ALARA) principles in diagnostic imaging (Laqmani et al., 2016).

2.4.2 Metrics used in CTPA

The measurement of radiation dose is usually reported in millisieverts (mSv). An important notice from the Code of Practice for Medical X-ray Equipment Users (Directorate Radiation Control, 2016) indicates that the effective radiation dose limit for the public in South Africa is 1 mSv per annum, and the effective radiation dose received for radiation workers is 20 mSv per annum. Moreover, radiation workers' effective dose should not exceed 100 mSv over five years or 50 mSv annually. However, the

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annual equivalent radiation dose to the skin is 50 mSv for the public and a relatively higher value of 500 mSv for radiation workers. The radiation dose of patients may vary substantially per radiological examination. The precise radiation dose depends on the CT scanning parameters, such as pitch and scan length, patient age, anatomy, gender, and stature. Therefore, it is impossible to accurately predict the radiation dose an individual patient will receive. In addition, patients' sensitivity to radiation may vary according to biological factors, such as age and gender (Directorate Radiation Control, 2016).

Dosimetric calculations for CT examinations are based on two quantities: volume-weighted dose index ($CTDI_{vol}$) and the dose-length product (DLP). The $CTDI_{vol}$ depends on the exposure factors, scan field of view, collimation, and pitch factor selections, whereas DLP also depends on the scan length (Tsalafoutas & Metallidis, 2011). The $CTDI_{vol}$ represents the dose through a slice of an appropriate phantom per gantry rotation, and is a weighted average measurement expressed in milligray centimetre ($mGycm^{-1}$). The DLP, on the other hand, is a measure of CT tube radiation output/exposure. It represents the applied radiation dose and accounts for the length of radiation output along the z-axis (the patient's long axis). It is calculated by multiplying the $CTDI_{vol}$ by the scan length in centimetres (Tsalafoutas & Metallidis, 2011).. According to a technical reference manual of General Electric Healthcare (2011), the DLP may also be defined as the product of the $CTDI_{vol}$ and the scan length for a group of scans. This number is summed over the entire examination to produce an estimated total dose, expressed in milli-gray centimetres squared ($mGycm^2$) (General Electric Healthcare, 2011: 20; Genena & Mohamed Selim, 2016).

A further measure of importance is the effective dose, which represents the stochastic health risk to a patient. Effective dose is, therefore, an important metric that is used to describe radiation detriment (Chen et al., 2020). The effective dose measurement gives a value that considers the given exposure condition, but not the characteristics of the patient. The effective radiation dose is estimated by determining the average energy deposited within each organ, multiplied by the organ's radio-sensitivity

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factor, and then summed for all the organs (Genena & Mohamed Selim, 2016). The effective dose is calculated by multiplying the DLP with the body-specific conversion factor (the k-factor) determined by Monte Carlo simulations for different body regions.

Calculating the different metrics is important, so that radiologists can adhere to the principles of ALARA. Knowledge of radiation dose is imperative for radiologists to comply with the principle. In particular, the radiation dose in neonates and children is greater than in adults (Newman et al., 2016). For example, the CT radiation dose to the head of a neonate is approximately 2.3–2.5 times more than an adult, and approximately 1.3–2.4 times more to the body compared to an adult. Newman et al. (2016) show that computing radiation dose varies according to different methods. Dose calculation methods must be properly documented to reduce unnecessary CT radiation doses, especially for children.

2.4.3 Contrast media in CTPA

Contrast media are a group of chemicals that have been developed to facilitate the characterisation of pathology for imaging. These chemicals improve the contrast resolution of an imaging modality. Various forms of CM have been used to improve medical imaging. Millions of radiological examinations are performed annually in the United States of America using intravascular CM (ACR, 2023). All intravascular iodinated CM is based on tri-iodinated benzene. There are three types of CM; the oldest form is the high-osmolar CM, the non-ionic compounds, and the most recent class of media, dimers of a molecule with two benzene rings (Murphy et al., 2016; Robbins & Pozniak, 2010). CM is a chemical substance with a higher atomic number than atomical structures such as bone and lung; therefore, it will increase the density of an organ's anatomical structures after administration. Different CM are available for radiological examinations, such as, angiography, venography, and

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fluoroscopy (Naufal, 2012). In CTPA, a CM is crucial to demonstrate the main pulmonary artery and its branches and abnormalities.

There are several methods to administer CM into the body. It may be administered orally, rectally, intravenously, intra-arterially, and mechanically. Its goal is to demonstrate the filling of a body cavity or partial space, intra-articularly and intrathecally. If the CM is to be injected, injection methods vary and depend on vascular access, differential diagnosis, and imaging examination type (ACR, 2023).

For CM administration, specifically during CTPA, a volume of 20 ml is used for bolus tracking, and it is normally documented in a collection sheet. The volume of CM will be calculated equal to the scan time delay and flow rate product. Therefore, reduced iodine concentration in the vessel will reduce the volume load of patients for CTPA examinations (Sudarski et al., 2019). If the visualisation of the pulmonary vessels is not well demonstrated, a second CM dose will be administered, and the examination will be repeated for accurate pulmonary vessel visualisation (Szucs-Farkas et al., 2010).

Using CM poses a risk for the patient. The most common mild side effects patients may experience from CM during an examination are nausea, vomiting, flushing, pain, or a metallic taste (BRACCO, 2009; Tecmed Pharma, 2015). Patients may also suffer cold or warm feelings and headaches that could become severe and last a few days. More severe side effects the patient may experience include tightness or difficulty breathing, skin rash, itchy spots or redness, fever, leg swelling, pain near or at the injection site, and seizures (BRACCO, 2009; Tecmed Pharma, 2015). In some instances, patients may require medical treatment if the symptoms persist or worsen after the administration of CM. Furthermore, some diseases or conditions could add to a patient's risk of having an adverse reaction to the CM; therefore, it is important to gather patient history (Robbins & Pozniak, 2010). These diseases or conditions include allergies, which could double the risk of an adverse reaction, anxiety, and asthma, which increases the risk of reaction to CM up to five times. Other diseases important to know about when administering CM are cardiac disease, diabetes, and gout. Dehydration can

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potentially increase nephrotoxicity, particularly in patients with impaired renal function or multiple myeloma. For patients who had had previous reactions to CM, the risk to have a recurrent reaction is potentially increased if CM is administered (Andreucci et al., 2014; Robbins & Pozniak, 2010).

2.4.4 Radiation protection in CT

With the extensive use of CT worldwide, there has been an increased focus on developing guidelines and protocols to ensure that CT is used appropriately and that the principles of ALARA are adhered to. The radiological community is working to reduce radiation exposure dose, particularly in young patients. Recent studies have shown a growing number of young adults with suspected PE (Szucs-Farkas et al., 2010). As a result, the International Commission on Radiological Protection (ICRP) introduced the concept of diagnostic reference levels (DRL) many years ago. In CT, DRLs are accepted as a tool for optimisation in diagnostic, interventional radiology, and nuclear medicine (Paulo et al., 2020). In 1997, the European Union formally introduced the concept and mandatory use of DRLs in every member state. Furthermore, the European Union has reinforced the obligation with review and use in 2013, through the Council Directive 2013/59/EURATOM (BSSD), on the protection of the health of individuals against the dangers of ionising radiation with medical exposure. DRLs are not intended for regulatory or commercial purposes (Paulo et al., 2020).

The development of most DRLs has been based on different anatomical locations. However, this approach has limitations, because, in CT, different clinical indications require different exposure levels for the same anatomical location (Paulo et al., 2020). For example, for a chest CT, the DRLs should be different for PE, lung cancer, or coronary calcium, because the requirements for the image quality parameters and scan length are different. Although the ICRP has suggested the clinical approach, the anatomical location approach is still mostly used (Vañó et al., 2017).

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In radiological practice, it is imperative to reduce radiation exposure dose where possible. Various low-dose tools can reduce patient risk; however, they depend on patient characteristics, the body region to be imaged, and the clinical indication (Szucs-Farkas et al., 2010). The low-dose option has the disadvantage that it could produce lower-quality images. Therefore, different countermeasures are often needed to prevent lower-quality images and loss of diagnostic power. Thus, CT scanning should only be performed when there is a clear medical necessity.

2.4.5 Quality assurance of CT equipment

To ensure the safety and protection of patients and healthcare workers, public and private radiology practices should be able to provide proof of properly installed, well-functioning diagnostic equipment. Therefore, the primary purpose of a quality control programme is to maintain and control the quality of diagnostic imaging in all diagnostic health facilities worldwide (Periard & Chaloner, 1996; Delis et al., 2017) and limit the radiation dose to the patient, and the number of repeat examinations.

In diagnostic imaging, regular equipment inspection will ensure a safe working environment. The following statement confirms the importance of the continuous optimisation of quality: "Know your unit, know its importance and be proud of what you do and know you make a difference" (General Electric Healthcare, 2011). Every radiology department should have an established quality control programme. As part of the quality control programme, quality assurance tests must be performed at three-monthly, six-monthly, and annual intervals, per the imaging product vendor used in these facilities. Quality assurance ensures early diagnosis of equipment problems, reduces equipment repairs, and maintains optimum performance (Mdoe & Msaki, 2006). Differently stated, quality assurance is an overall management plan to guarantee the efficacy of data to optimise the service delivered to the patient. The aim is always to obtain high-quality images consistently (National Quality Assurance Coordinating Group for Radiography, 2006) and keep the radiation dose to the patient as low as possible.

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To achieve optimal image quality for the CT scanner, quality assurance is fundamental to ensuring that the patient's radiation dose is limited and repeat examinations are minimised. For any CT machine, the quality assurance programme begins with start-up baseline performance data acquired during installation, or after repair or replacement of an X-ray tube, collimator, detector, and data collection system. Daily quality assurance information is obtained by scanning a known material (usually a phantom) provided by the specific vendor under a prescribed set of conditions. Daily calibration scans of air and uniform objects within the phantom provide baseline information for the system to produce patient images. The system uses calibration data for kilo voltage (kV), detector row thickness, focal spot size and scan fields (General Electric Healthcare, 2011). The result of the phantom scan is compared with results previously obtained or optimum values from the initial quality assurance test done by the General Electric vendor. The tests are repeated daily to detect changes in image quality values and to note scanner problems.

Detection of image quality degradation or quality assurance value changes should be reported to the service technician, who must perform a more detailed test. Early intervention could prevent a major breakdown, a decrease in the quality of the images or unnecessary radiation dose to the patient (General Electric Healthcare, 2011). Thus, establishing and maintaining a regular quality assurance programme is paramount for maintaining consistent image quality over the lifetime of the system. Consistent system testing should be followed by the facility's specific quality assurance programme (General Electric Healthcare, 2011).

2.5 D-dimer assaying in PE diagnosis

The optimal diagnostic strategy for patients with suspected PE is constantly under review. Because population age is increasing, especially in the West, diagnosing and treating PE has become a significant challenge (Kubak et al., 2016). In the emergency department, the correct and timely

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identification of PE remains a significant diagnostic challenge for emergency physicians, largely because of its non-specific clinical presentation (Salehi et al., 2021). It is imperative to exclude PE, because of the bleeding risks of anticoagulation and the costs associated with treatment and monitoring (Patel et al., 2020). Therefore, patients undergo cost-effective initial tests with low risk to exclude PE efficiently. In particular, today, D-dimer assays are extensively used routinely to exclude PE (Lippi et al., 2014; Van der Hulle et al., 2016; De Wit et al., 2022).

D-dimers were identified in the 1970s for the assessment of disseminated intravascular coagulation. D-dimers are produced by the fibrinolytic system and are used as indirect biological markers of thrombotic activity (Tuck et al., 2021). D-dimers are produced during thrombus generation, by first cleaving fibrinogen by thrombin to produce fibrin monomers. These monomers then form polymers through the action of factor XIIIa, which crosslinks adjacent D-domains. After that, plasmin releases the D-dimer molecules during the degradation of fibrin clots. These intravascular D-dimers are a good indication of thrombus formation (Szigeti, 2014; Weitz et al., 2017). Initially, laboratory tests could not distinguish between fibrinogen and products of fibrin degradation; but by using monoclonal antibody-based assays, D-dimers could be measured (Tuck et al., 2021). Later, improvements were made to the D-dimer tests, which included enzyme-linked immunofluorescent immunoassays (EIFAs), microplate enzyme-linked immunosorbent assays (ELISAs), and latex agglutination quantitated tests (Sumney & Whiteman, 2007).

Multiple evidence-based algorithms and decision rules have been used to plan and optimise diagnostic options for PE. However, studies have found that emergency physicians seldom use decision rules, because of rule complexity, credibility, and local culture (De Wit et al., 2022). Furthermore, a barrier to using newer decision rules is that they need to be independently, prospectively, and externally validated, particularly in the United States of America. Conventional algorithms apply a Bayesian approach with an initial estimate of a pretest probability, D-dimer testing

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in patients with non-high clinical probability, and if a patient has a D-dimer level above a specific threshold, chest imaging, CTPA, or V/Q is performed (Freund et al., 2021). Most manufacturers and institutions use the threshold of 500 µg/L, because several studies demonstrated a 100% sensitivity for the test (Tuck et al., 2021). However, this threshold is highly non-specific (Di Nisio et al., 2007), and many other conditions have similar results, including malignancy, haemorrhage, trauma, sepsis (Wells, 2007) and, more recently, COVID-19 (Yong et al., 2020; Masselli et al., 2021). A study published in 2016 by Kubak et al. investigated 1 051 CTPAs for a possible correlation between D-dimer levels and location of PE and found that 216 (21%) showed PE. There were associated D-dimer analyses in 822 of the CTPA examinations. The threshold of 0.5 mg/L used in this study achieved a sensitivity and negative predictive value (NPV) of 99%. The age-adjusted cutoff achieved a sensitivity and NPV of 98%, and the suggested cutoff of 0.9 mg/L achieved a sensitivity and NPV of 97%. They concluded that the elevated D-dimer cutoff of 0.9 mg/L achieved a high sensitivity and NPV while reducing the number of CTPA by 27%, and that there is a correlation between D-dimer values and PE. In a systematic review of 61 studies, pooled estimates showed a D-dimer sensitivity of 0.97 and a specificity of 0.41, and for CTPA, a sensitivity of 0.94 and a specificity of 0.98 (Patel et al., 2020). This study found that the D-dimer test was more sensitive than CTPA.

2.6 Role of SARS-CoV-2 in PE

In December 2019, a novel virus, the severe respiratory syndrome coronavirus (SARS-CoV-2), was identified in Wuhan, China, which developed into a global pandemic with widespread repercussions. The pandemic of the coronavirus and the associated disease, COVID-19, reached the African continent late in February 2020 (Li et al., 2020). Coronavirus is a highly contagious, transmissible virus with high morbidity, and results in rapid onset of widespread inflammation, a potentially fatal disease (Li et al., 2020; Shi et al., 2020). This virus is a single-stranded ribonucleic acid virus with characteristic

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spike S-proteins. The clinical presentation of COVID-19 is associated with severe respiratory systemic inflammation, giving rise to fatigue, dyspnoea, coughing, fever, hypoxia, myo-arthralgia, anoxia, elevated D-dimer levels, and loss of taste (Li et al., 2020). However, the mediated transmission of SARS-CoV-2 to humans remains unknown, as it is thought to have its origin in bats (Li et al., 2020).

Coronavirus disease affects mainly the respiratory system, which may manifest as viral pneumonia in some patients. The human respiratory epithelial cells are infected by interacting with the angiotensin-converting enzyme 2 receptor and the viral S protein in a human cell (Ni et al., 2020). This infection can lead to the overactivation of the body's immune system, resulting in pulmonary fibrosis and respiratory failure (Tuck et al., 2021). The high mortality rate of COVID-19 results from a few pathological processes, including diffuse alveolar damage, venous thromboembolism, superadded bacterial infection, and heart failure. Several studies found that the risk for PE and venous thrombosis is higher in patients suffering from more severe forms of the disease (Rothzinger et al., 2020; Masselli et al., 2021).

The rapid spread of COVID-19 necessitated the identification of prognostic factors. Several laboratory tests were suggested to predict mortality, one of which is the D-dimer assay (Tuck et al., 2021). Because of the increased incidence of COVID-19-induced thromboembolic disease, the use of D-dimer assays also increased rapidly. This culminated in many COVID-19 patients with a low clinical suspicion of PE undergoing D-dimer tests. This increased CTPA examinations, which increased patients' risk from CM and radiation exposure (Gervaise et al., 2020). Tuck et al. (2021) studied D-dimer use in admissions during the peak of the pandemic to establish sensitivity in diagnosing pulmonary PE. Patients without COVID-19 infection were equally as likely to have evidence of PE as COVID-positive patients were. However, the sensitivity of the D-dimer test was higher in COVID-positive patients at a lower D-dimer level (>1 500 µg/L, sensitivity 81%, specificity 70%) than in those without clinical, immunological, or radiological evidence of COVID-19 infection

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(D-dimer >2 000 µg/L, sensitivity 80%, specificity 76%) (Tuck et al., 2021).. These data suggest higher D-dimer threshold levels for the exclusion of PE.

The management of COVID-19 patients is complicated. The heterogeneity of the coronavirus disease has caused major challenges for healthcare providers and for the management of patients diagnosed with the disease (Rothzinger et al., 2020). Due to the increasing number of COVID-19 infections, more patients presented with increased D-dimer levels and chest pain. The increased D-dimer levels and chest pain presentation gave rise to a greater number of requests for CTPA at the radiology practice where this investigation was conducted.

The first-line imaging tool in suspected COVID-19 infections is a chest image radiograph to evaluate the lung fields. However, CT has become the fundamental diagnostic tool for managing and following up on COVID-19 patients; it also provides imaging findings of the different stages of COVID-19 disease and increases understanding of its progression in the respiratory system, i.e., in COVID-19 pneumonia as observed in the private practice. Generally, when CT imaging is requested, the examination should be performed with as little harm as possible to the patient. This implies that contrast media injection should only be administered when needed to prevent possible renal insufficiency and allergic reactions (Rothzinger et al., 2020). According to Gervaise et al. (2020), non-contrast CT chests played an essential role in COVID-19 pneumonia evaluation. CT chest imaging is more sensitive than non-imaging tests, such as reverse transcription polymerase chain reaction. Furthermore, it is highly specific in an epidemic context in correspondence with COVID-19 and PE diagnoses. The assessment of the severity of pulmonary involvement is demonstrated with contrasted chest studies and could play a role in evaluating therapeutic efficacy in combination with clinical information (Gervaise et al., 2020).

In cases where COVID-19-related complications arise, such as PE, a CTPA is requested. As COVID-19 causes microvascular injuries associated with the pro-coagulant state of COVID patients, a study by Gervaise et al. (2020) confirmed the association between acute pulmonary emboli in hospitalised and

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COVID-19 patients, but pulmonary emboli were also diagnosed in non-hospitalised COVID-19 patients who were referred for CTPA. CTPA is used for the diagnosis and follow-up evaluation of a patient with COVID-19; CTPA requests rapidly increased during the COVID-19 pandemic. CTPA examinations were only used to determine the presence or absence of PE and to observe the lung parenchyma tissue condition and the disease progression radiologically. However, CTPA is used to demonstrate acute pulmonary emboli, as COVID-19 patients possess an increased risk for acute PE. Masselli et al. (2021) report that COVID-19 patients in the intensive care unit who are critically ill have a significantly higher rate of venous thromboembolism and thrombosis.

2.7 Conclusion

The frequency of PE in the Western world is increasing, particularly among young adults. Because of the life-threatening nature and ambiguous symptoms of PE, it is imperative to optimise its timely diagnosis. Although CTPA has high sensitivity and specificity in diagnosing PE, it has a radiation penalty and expense. Therefore, the inclusion of non-invasive, low-cost predictive testing has become an essential tool in the PE diagnostic workup of patients. D-dimer assays are currently used as a predictive tool for suspected PE and for referring patients to CTPA. Because not all patients with elevated D-dimer levels present with PE, it is important to gain an understanding of the relation between elevated D-dimer levels and a positive PE diagnosis, to avoid patients being exposed to radiation unnecessarily.

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Chapter 3

Study Design, Materials and Methods

3.1 Introduction

In a private radiology practice in Bloemfontein, computed tomography pulmonary angiography (CTPA) is the primary imaging method used to diagnose pulmonary embolism (PE). Clinicians usually refer patients with elevated D-dimer levels in the blood, and/or chest pain for CTPA imaging to assess whether PE is present. This study was, thus, undertaken to ascertain what the relation is between elevated D-dimer levels in the blood and confirmed PE. Patient data for this retrospective study were collected from the picture archiving and communication system (PACS) at the participating private radiology practice in Bloemfontein. Because this study commenced shortly before the onset of the COVID-19 pandemic, it was decided to include patients with elevated D-dimer levels and suspected COVID-19. Therefore, the main research question to be answered in this study was:

> *What is the relation between an elevated D-dimer test and a positive CT pulmonary angiogram to confirm PE?*

To answer this question, the following objectives were devised:

1. To design a novel data capturing instrument (DCI) for data related to elevated D-dimer levels and a positive PE diagnosis following CTPA (based on review and literature and PACS data categories);

2. To evaluate the suitability of the newly designed DCI (using focus group discussion with CT expert, and pilot study);

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3. VosTo determine the relation between elevated D-dimer levels and positive PE diagnosis following CTPA (this would be achieved through data analysis).

3.1.1 Sample method

According to Burns and Grove (2005), sampling involves selecting a group of people, events, behaviours, or elements from a given population to conduct a study. A sampling plan defines the selection process, and the sample denotes the selected group of people or elements included in a study. A random sampling method was used to select the sample size of 10 CTPAs meeting the inclusion criteria, specifically to pilot the data capturing instrument (DCI).

3.1.2 Study population

The study population comprised all patients referred for CTPA examinations for suspected pulmonary PE to the private radiology practice between January 2019 and December 2020. The study included all the patient data for this specified period that met the inclusion criteria.

3.2 Study design

The study was a retrospective, descriptive study using quantitative data. A descriptive study design describes a situation accurately and carefully as it accumulates data in the original environment (Uys & Basson, 2005). The data are generally analysed and described through frequency, central tendency, and dispersion (De Vos et al., 2012). However, using a quantitative approach, numerical data are analysed using statistical procedures (Polit et al., 2001). Patient radiology reports were examined in the private radiology practice to ascertain if a relation existed between patients' elevated D-dimer levels and a positive diagnosis of PE with CTPA. The study design was chosen due to the fact that not all patients could give written or verbal consent.

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This research study comprised three major research phases. In Phase 1, a data capturing instrument (DCI) was designed to capture the existing digital data of patients, which was stored on the PACS in the private practice. After designing the DCI, the DCI was evaluated for suitability and for recording the relevant patient data in phase 2. Once all patient data had been captured, it was analysed and interpreted to answer the research question, namely whether there exists a relationship between elevated D-dimer levels in the blood and the presence of PE.

3.2.1 Study location

The research project was conducted in a private diagnostic radiology practice in Bloemfontein, in the Free State province of South Africa. Patients are served at this practice 24 hours a day by several radiologists and more than 30 radiographers. The practice provides diagnostic imaging and interventional procedures, including bone density scans, magnetic resonance imaging (MRI) scans, CT scans, fluoroscopy, X-rays, mammography, and ultrasound. In this practice, the CT unit used for CTPA examinations is a General Electric (GE) Light Speed (VCT) 64-slice multi-detector scanner that was installed in 2013. In this practice, the CT scan parameters used for CTPA were mostly according to the Light Speed volumetric scan parameter protocol stated in the General Electric technical reference manual (General Electric Healthcare, 2011) and a few additional settings (Table 3.1).

Table 3.1 CT parameter settings for CTPA

CTPA GE Light Speed Protocol	
Scanner type (rows)	Single source (64)
Collimation	64 × 0.625 mm
Rotation time	0.6 s
Pitch	0.984:139.37

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Bolus Tracking Region of Interest (ROI) location	Pulmonary trunk
Auto-trigger-threshold	20 Hounsfield units (HU)
Monitoring scans	30 images
Tube voltage	100 kV
Tube current modulation	On (Modulation transfer function)
Scan direction	Craniocaudal
IV catheter size	20 Gauge
CM iodine concentration	370 mg ml^{-1}
CM flow	5 ml s^{-1}
CM bolus amount	80 ml
Sodium chloride flow	5 ml s^{-1}
Sodium chloride bolus amount	58 ml
Iodine delivery rate (IDR)	1.4 gl s^{-1}
Additional settings at the private practice	
Detector collimation	40 cm
Gantry rotation	0.5–1.0 s
Slice thickness	0.625 mm
Slice interval	0.625 mm
Reconstruction algorithms	Standard window, Lung window
Reconstruction slice thickness	1.25 mm
Reconstruction interval thickness	5 mm

Contrast media (CM) administration to patients for CTPA was performed according to the manufacturer's specifications. Two types of non-ionic iodinated CM were used routinely at the research site. Either Scanlux 370 (pharmaceutical name Lopamidol) mg ml^{-1} or Imeron 400

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(pharmaceutical name Iomeprol) mg ml^{-1} were injected intravascularly into patients with a dual-head injector pump at a flow rate of 4-5 ml s^{-1} (Tecmed Pharma, 2015). A bolus tracking technique was used to enhance the main pulmonary artery to calculate the amount of CM required for a patient. Before applying the bolus tracking technique, the pulmonary artery was first visualised by administering 20 ml of CM and 20 ml of saline as a bolus chaser. Once the pulmonary artery was enhanced, the bolus timing sequence was used to determine the volume of CM and scan time. Thereafter, CTPA imaging was accomplished in the helical scanning mode. The whole chest and lung fields, as well as the upper part of the liver, were included in a scan. After the CTPA examination, the radiologist received the reconstructed CT images and reported on these images. The report and the reconstructed CT images were sent to the radiology PACS to allow the referring physicians to access their patients' CTPA images and results (General Electric Healthcare, 2011). This report and reconstructed images are then sent to the radiology PACS, so that referring physicians can access their patients' CTPA results and images (General Electric Healthcare, 2011).

3.2.2 Study population

The study target population comprised all patients referred for a CTPA examination for suspected PE who had been referred to the private radiology practice from January 2019 to December 2020. The size of the study population after applying the inclusion and exclusion criteria, referred to as the sample population in this study, was 1 219 patients (Table 3.2). Patients older than 85 years were excluded because their veins are usually thin and fragile and cannot withstand the high flow rate of the CM injection, which could damage the veins of the patient. In the event of vein damage, the CM injection will have to be repeated. Pregnant patients were excluded from the study to prevent foetal radiation exposure; they are usually referred for an alternative test, such as a pulmonary ventilation-perfusion (V/Q) scan. V/Q scans have a 50-fold lower radiation dose to the breast (0.28–0.9 versus

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50–80 mSv in 64-slice CT scanners) and use a low-dose CT technique to perform perfusion scans (Moore et al., 2018).

3.2.2.1 Inclusion criteria

All male and female patients aged 18 to 85 years who had been referred for CTPA examinations were included. In addition, since 2020, CTPA requests included COVID-19 patients with positive and negative COVID-19 test results; therefore, these patients were also included in the research study. The study sample included all patients referred to the private radiology practice for CTPA with an elevated D-dimer test, chest pain and COVID-19 positive and negative test results between January 2019 and December 2020. In addition, patients referred for CTPA with previous CM allergic reactions and hypersensitivity to CM and who had had allergy preparation before the CTPA examination, and patients with renal impairment following dialysis treatment after CM administration were also included.

3.2.2.2 Exclusion criteria

All patients under the age of 18 years and over the age of 85 years were excluded from the study because their veins are very thin and fragile – the CM is required to be injected at a high flow rate. Using a high injection pressure often damages the veins and, for this reason, the injection will have to be repeated. In addition, pregnant patients were excluded from the study to prevent foetal radiation exposure. In such cases, an alternative test such as VQ scans may be used for pregnant patients. According to Moore et al. (2018), VQ scans have a 50-fold lower radiation dose to the breast (0.28-0.9 versus 50-80 mSv in 64-slice CT scanners). In addition, VQ scans use a low-dose CT technique to perform perfusion scans.

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Table 3.2 Inclusion and exclusion criteria used to select patient data on the PACS

Inclusion criteria	Exclusion criteria
Male and female patients aged 18 to 85 years	Pregnant patients
Patients referred for CTPA	Information about the radiation dose the patient received was missing Information about the type and volume of CM was missing

After applying the inclusion and exclusion criteria, the sample population included several groups of patients. The sample included all patients who had been referred to the practice for CTPA with an elevated D-dimer test, chest pain and COVID-19 (positive and negative test results). In addition, patients referred for CTPA with previous CM allergic reactions and hypersensitivity to CM who had had allergy preparation before the CTPA examination were also included. Patients with renal impairment following dialysis treatment after CM administration were also included.

3.3 Materials and methods

The research study was executed in three phases. In the first phase, a DCI was designed to guide the data-capturing process, using available patient data on the PACS. In the second phase, the DCI was applied to capture the available patient data. In the final phase, the data were analysed statistically, and a conclusion could be reached whether a relation existed between elevated D-dimer levels in the blood and a positive diagnosis of PE after CTPA.

3.3.1 Phase 1: Data capturing instrument design

During the design of the DCI, a two-step approach was followed. In the first step, the data capturing variables of the instrument were identified and then used to construct a draft instrument. In the second step, the draft DCI was tested. In the design step of the DCI, an extensive review of the

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literature was undertaken to establish what type of information should be captured. At the same time, the PACS was assessed to determine what different data categories were available to be used for the DCI, so that the research question about the relation between elevated D-dimer levels in the blood and a positive diagnosis for PE on CTPA could be answered. After the review of the literature and the PACS, the draft DCI was constructed. This draft DCI was evaluated by a focus group consisting of two radiographers. Both radiographers had more than 10 years of theatre angiography and CT angiography experience. The focus group method was selected to assist the researcher in gathering as much information as possible, exchange information, and assist the researcher to concentrate on specific variables to produce a reliable, focused DCI. A final credible DCI was formulated to collect the data for the research study.

The draft DCI was piloted to test whether the draft DCI contained suitable variables for capturing the patient data. This pilot was undertaken to identify flaws or assessment time requirements (Polit & Beck, 2008). The draft DCI was used to capture patient data of 10 randomly selected CTPA patient entries on PACS. The data of every tenth patient in the PACS, starting at patient 1, were used in this pilot. The data of each patient were first scrutinised to ensure that a referral letter and a radiology report were present, before the draft DCI was applied. If the data were incomplete, the next tenth patient entry in the PACS was assessed. The patient data collected during the pilot study were used to identify if any corrections or adjustments should be made to the DCI. This pilot study revealed that the DCI required no further changes and could be used to capture patient data for the main study. The data of the 10 patients of the pilot study were included in the main study (Polit & Beck, 2008; Botma et al., 2010).

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3.3.2 Phase 2: Data capturing

The CTPA patient data on the PACS were accessed with a login code. The CTPA patient data were then systematically assessed, one by one, to ascertain if they complied with the inclusion and exclusion criteria (Table 3.2). A unique number was awarded to each patient with compliant data. These numbers were listed separately so that the data could be verified for accuracy. A list was compiled containing the compliant patient's unique number. Of the available patient data on the PACS, the data of 56 patients were excluded, of which 26 patients were younger than 18 years and 26 patients were older than 85.

Furthermore, the patient data of nine patients were excluded because of the absence of radiation dose and CM information. The compliant patient data were then captured individually on separate printed DCI sheets. The data for each patient were anonymised by removing all personalised information. After capturing all the patient data, the data were transferred to an Excel spreadsheet with the different variables of the DCI. After capturing the data on the Excel spreadsheet, the data were checked for accuracy, duplication, and missing data by comparing the DCI sheets against the Excel spreadsheet and the PACS (Figure 3.1), as well as against the list of patient numbers. This was accomplished with the assistance of two fourth-year radiography students, who were busy with their workplace learning. The students underwent a training session about the data-capturing procedure. The students who assisted signed a non-disclosure form to ensure that patients' information and the study data were protected and kept confidential.

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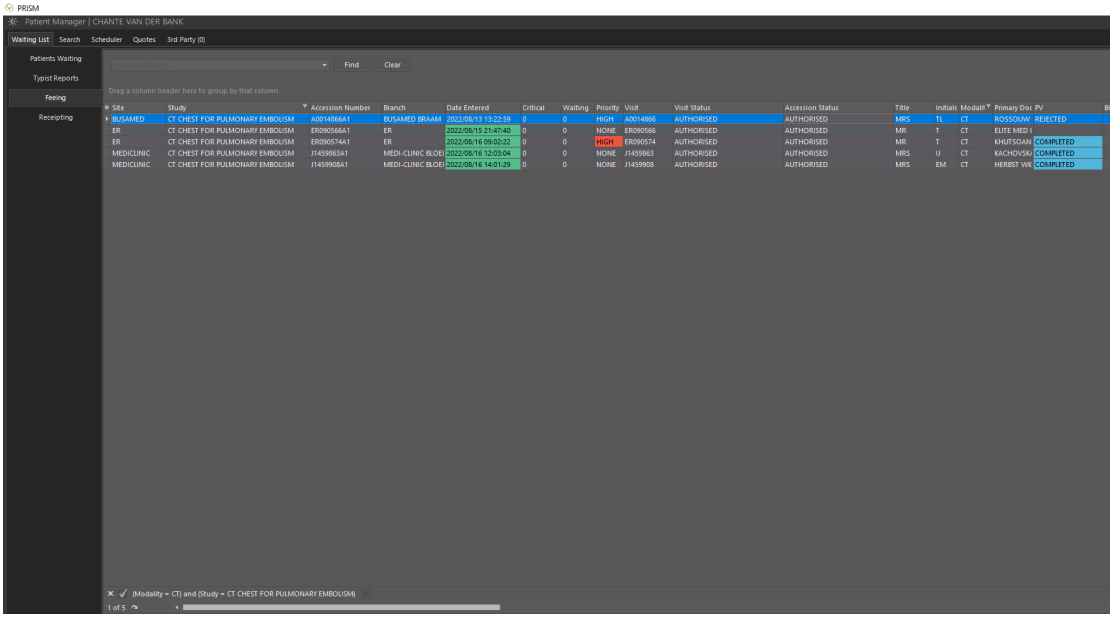

Figure 3.1 Extract of the data of several patients for CTPA on PACS

The data of several patient categories were captured from the PACS by this study. These categories included patients with elevated D-dimer levels and patients with a positive diagnosis of PE after CTPA. Other categories included patients with chest pain, ancillary clinical indicators (additional findings), and COVID-19 diagnoses. Figure 3.3 provides a flow diagram depicting the patient categories studied.

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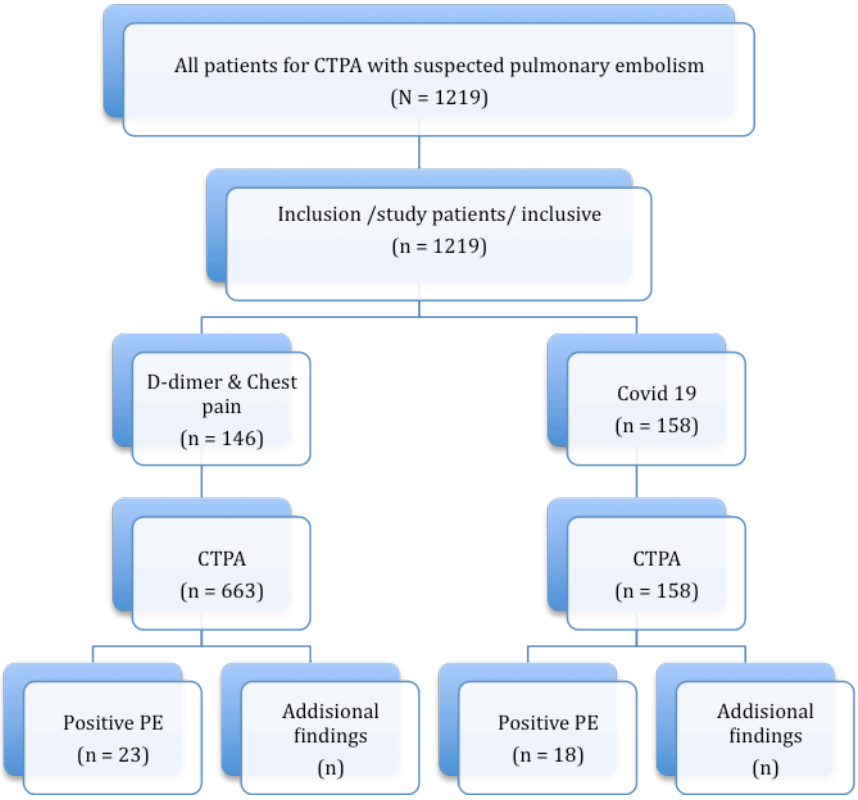

Figure 3.2 Flow diagram of the breakdown of the patient categories in this study

3.3.3 Phase 3: Data analysis

After collecting and capturing the data of the different variables listed in the DCI on Excel spreadsheets, the data were statistically analysed using SAS Version 9.4 software. The data variables included biographical information, clinical indicators, and imaging condition values. The summary statistics means, percentages, and ranges were calculated. Shapiro-Wilk tests were performed on the data of several variables to test whether the population data of the variables were normally distributed. The null hypothesis for normality was tested at a significance level of α = .05. Chi-square tests of independence were performed to ascertain if a relation existed between elevated D-dimer levels in the blood and a positive PE diagnosis after CTPA. These tests were performed on different clinical indicator groups composed of D-dimer and PE levels for the sample population and several subpopulations at a significance level of α = .05.

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3.4 Validity and reliability

Several quality control steps were taken to ensure the trustworthiness and quality of the data and the results of the study. The validity and reliability of the data and results of this study were ensured by using a tested DCI. The DCI was tested so that it could be used to accurately (valid) (Burns & Grove, 2005) and consistently (reliable) (Polit & Beck, 2008) capture patient data from the PACS. To ensure the validity and reliability of the data further, all captured data were checked for accuracy, duplication, and missing data by two fourth-year radiography students. Furthermore, data were analysed using standard statistical tests.

Several quality assurance measures were in place in the participating radiology private practice. All CTPA examinations were performed with a standard CTPA imaging protocol and CT scanner technical parameters to ensure the captured patient data recorded in the PACS was reliable. All CT radiographers applied the same standard CT protocol for CTPA imaging, using specific values for the CT scanner parameters, including slice thickness, pitch, automatic tube current modulation, and kV. As a result, each patient for CTPA obtained an accurate mAs dose based on their body stature size using a set kVp value. The CT scanner had a recorded list of services, quality assurance and standardised protocols used in CTPA imaging execution (Appendices E, F, G, H). The results calculated and received from the CT scanner were transferred to the reporting PACS used by a qualified radiologist.

3.5 Confidentiality

Confidentiality in this study was ensured by anonymising all patient data. Anonymising patient data ensured that patient data that were collected could not be linked to a specific individual; therefore, all patients' identities were kept confidential. Removing patient identifying information and using a

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numbering system achieved patient confidentiality. A specific unique identification number was allocated to each patient in the sample population. No personal information of any of the patients was recorded during data collection. The data was securely stored and password-protected on an external hard drive, which was then locked in a safe place. To always keep all patients' data secure and private, the researcher used a laptop that required a password to gain access.

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Chapter 4

Data Capturing Instrument

4.1 Introduction

A data capturing instrument (DCI) was designed to capture patient data from the picture archiving and communications system (PACS) to determine the relation between elevated D-dimer levels in the blood and computed tomography for pulmonary embolism (CTPA), to confirm the presence of pulmonary embolism (PE). The DCI was designed following an extensive review of the literature and input from experts. Thereafter, the DCI was piloted, so that the patient data would be accurately and consistently captured from the PACS.

4.2 Data capturing instrument

A DCI was designed to capture the patient data on the PACS. It comprised four major sections (Table 4.1). The first section of the DCI was used to provide patient biographical information, with the exclusion of information that would identify patients, to ensure patient anonymity. The other sections were used to generate specific information about D-dimers, CTPA and clinical findings mentioned in the radiologists' reports.

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Table 4.1 Sections of the data capturing instrument

Sections of DCI	Description	References
Patient biographical information	The patient's age, weight, and gender	Data in the health sector (HealthIT.gov, 2022).
CTPA imaging conditions	The CT scan parameters, as well as the CM type and volume, were included in this section	Pathak et al. (2011); Doğan et al. (2015) and through consultation with a focus group, drafted and tested
Clinical indicators	Clinical indicators that relate to PE and D-dimer levels were included in this section	Moore et al. (2018)
Ancillary clinical findings and abnormalities	During the data capturing using the DCI, additional clinical findings that relate to PE and D-dimer levels were documented	Liu et al. (2015); Dorfman (2016); Stein et al. (2020);

4.2.1 CTPA imaging conditions

The CTPA imaging conditions of the DCI comprised a section to generate information on CT scan parameters and scan time, and a section to generate information on the contrast media (CM) used during CTPA. The values of several CT scan parameters were recorded and included the values of tube voltage (kVp) and tube current (mAs) (Table 4.2). Similarly, several scan time values were recorded, including the CT dose metrics, computed tomography dose index volume (CTDIvol) and dose length product (DLP). Both the CM brand and strength were also recorded with the DCI.

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Table 4.2 **CTPA scan parameters and contrast medium type and volume captured by the DCI**

CTPA imaging	Value units/Quality
1. CT scan parameters	
Tube voltage	kVp
Scan dose reduction	%
Tube current modulation	On/Off
Tube current	mAs
mA quality factors	Noise index, Smart mA, mAs/slice
2. Scan time	
Scan length	Start and end positions
Rotation time	s
Pitch and speed	mm/s
Beam collimation	mm
Number of scan phases	Up to a maximum of 6
Total CTDIvol	mGy
Total DLP	$mGycm^{-1}$
Scan field of view (SFOV)	mm
Slice thickness	mm
3. Contrast medium	
Brand and strength	
Volume	ml

4.2.2 Clinical indicators

The DCI also comprised a section to obtain patient clinical information. Some of the indicators listed in the DCI related directly to PE, for example, chest pain (Table 4.3). In addition, the previous patient

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history of PE, gathered from the patient referral letter, was also included in the DCI, because the patient's history often sheds light on their current health status, past events, and other signs of PE. All the clinical indicators were measured according to their presence or absence (Yes/No). This section also made provision for recording data about the presence or absence of SARS-CoV-2 and related clinical presentations and patient outcomes.

Table 4.3 Patient clinical indicators captured by the DCI

Patient clinical indicator	DCI Measurement
Chest pain	Yes/No
Increased D-dimer level	Yes/No
Previous history of PE	Yes/No
COVID-19 positive	Yes/No
Post 10 days COVID-19 test	Yes/No
COVID-19 outpatient	Yes/No
COVID-19 hospitalised patient	Yes/No
COVID-19 ventilated patient	Yes/No

4.2.3 Ancillary clinical findings and abnormalities

The DCI also provided sections to generate information about the patient's clinical condition and radiological findings. A section was included to record ancillary clinical findings, such as nodules or a mass (Table 4.4). Another section was included to record information about abnormalities mentioned by the radiologist, for example, in the heart and vasculature. All the clinical findings or abnormalities were measured according to their presence or absence (Yes/No).

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Table 4.4 Ancillary clinical findings and abnormalities captured by the DCI

Ancillary clinical findings/abnormalit	DCI Measurement
1. Ancillary clinical finding	
Pulmonary hypertension	Yes/No
Pleural effusion	Yes/No
Nodules	Yes/No
Mass	Yes/No
Ground-glass opacification	Yes/No
Lymphadenopathy	Yes/No
2. Clinical abnormality	
Heart	Yes/No
Vasculature	Yes/No
Thyroid	Yes/No
Visualised abdomen	Yes/No
Visualised bone	Yes/No

4.3 Pilot test results of DCI

After the DCI was designed, it was tested to determine if it contained all the relevant variables to capture patient information for this study. The DCI was tested using the PACS data of 10 randomly selected patients from the sample population. The PACS data of each patient was then scrutinised and captured in the Excel spreadsheet design of the DCI. During the testing of the DCI, it was found that all relevant variables were present, and that the DCI could be used to capture the patient data for this study effectively.

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4.4 Discussion

After the literature had been reviewed, a focus group discussion was held, and a pilot study undertaken, the DCI was deemed appropriate for collecting patient data stored in the PACS. The DCI comprised four major sections, namely a section to gather patient demographical information and sections to capture data about CTPA imaging conditions, clinical indicators and ancillary clinical findings and abnormalities. This newly designed DCI recorded more than 30 variables and was applied to capture patient data from the PACS to determine the relation between elevated D-dimer levels and a positive CTPA.

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Chapter 5

Relation between D-dimer and PE confirmation with CTPA

5.1 Introduction

After the data capturing instrument (DCI) was designed, it was used to capture patient data from the picture archiving and communications system (PACS) at the private radiology practice in Bloemfontein. These data were then used to determine the relation between elevated D-dimer levels in the blood and a positive pulmonary embolism (PE) diagnosis after computed tomography pulmonary angiography (CTPA). The relation between elevated D-dimer levels and a positive PE diagnosis was studied in several population groupings. Firstly, this relation was studied in the sample population of 1 219 patients, which made up all patient data of the study. Thereafter, this relation was studied in three subpopulations of the sample population, namely,

1. The subpopulation comprising all patient data, excluding the COVID-19 patient data;
2. The subpopulation comprising data of patients with a history of PE; and
3. The subpopulation containing the data of COVID-19 patients.

5.2 Biographical patient statistics

To obtain an understanding of the biographical characteristics of the patient population (n = 1 219) in this study, summary statistics were calculated for age, gender, and weight. A Shapiro-Wilk test was performed to investigate the distribution of data. The test revealed that the age distribution was not normal (W = 0.980, p <0.0001). The median age of the sample population was 57 years, while the median age of the lower quartile was 45 and the upper quartile 70 years (interquartile range 45 to 70

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years) (Figure 5.1 A). Similar to the age distribution, the Shapiro-Wilk test showed that gender distribution was not normal (W = 0.980, p <0.0001). Approximately two thirds of the sample population were female (Figure 5.1 B). The weight of most patients in the sample population was ≤100 kg (Figure 5.1 C).

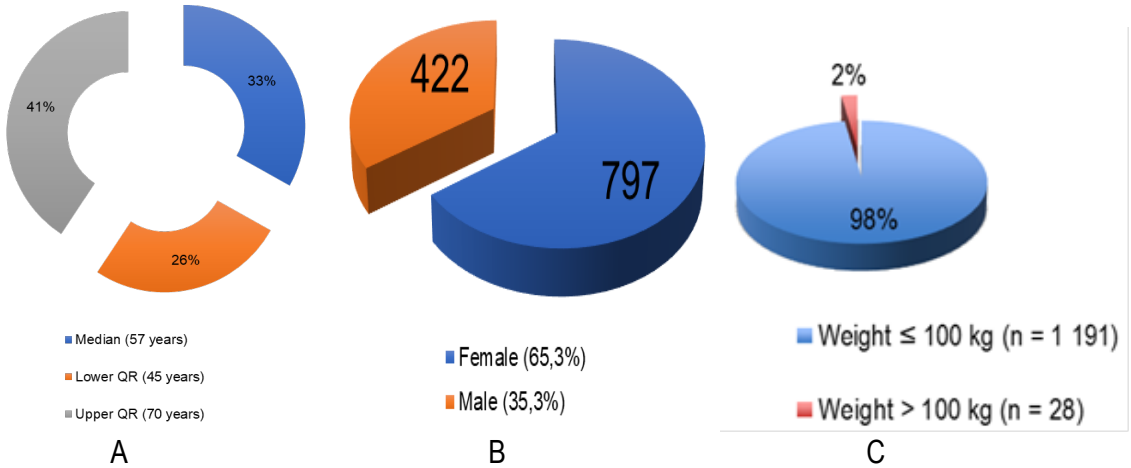

Figure 5.1 Distributions of biographical data of CTPA patients A. Age, B. Gender, C. Weight

5.3 CTPA imaging information statistics

The imaging information of the sample population corresponded with many of the CTPA imaging parameters. All the CT scan parameters were the same across the sample population (Table 5.1). Although many scan time parameters had fixed values, the number of scan phases differed amongst the patients. Because the start and end positions differed amongst the patients of the sample population, the scan length and DLP values also differed across the sample. The preferred CM in this study was Scanlux 370 (more than 70% of the patients). The data revealed that the median injection rate when using Scanlux 370 was, for the most part, lower than the injection rate used for Imeron 400.

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Table 5.1 Number of patients at different levels of CTPA imaging and description of distribution

CTPA imaging	Quantity/Quality	n	Normality	
1. CT scan parameters			W value	p-value
Tube voltage	120kVp	1 219		
Scan dose reduction	30%	1 219		
Tube current modulation	On	1 219		
Tube current	Smart mA	1 219		
mA quality factors	Noise index = 25	1 219		
	2. Scan time			
Scan length	Start and end positions	1 219	Start position: 0.577 End position: 0.946	<0.0001 <0.0001
Rotation time	0.6–0.7 s	1 219		
Pitch and speed	Pitch: 0.984 mm Speed:139.37 mm s-1	1 219		
Beam collimation	64 × 0.625 mm	1 219		
Number per scan phases	3 4 5 6 7	4 125 952 137 1		
Total CTDIvol	mGy (CTDIvol is different for each phase)			
Total DLP	$mGycm^{-1}$		0.909	< 0.0001
Scan field of view (SFOV)	32 mm	1 219		
Slice thickness	0.625 mm	1 219		

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CTPA imaging	Quantity/Quality	n	Normality	
1. CT scan parameters			W value	p-value
	3. Contrast medium			
Brand and strength	Scanlux 370	1 189	0.795	< 0.0001
	Imeron 400	30	0.907	< 0.0001
Volume	Scanlux 370: Median; 75 mls^{-1}	1 189		
	Imeron 400: Median: 80 mls^{-1}	30		

5.4 Clinical information statistics

The clinical information statistics were gathered from the PACS of the sample population for eight clinical indicators. Few patients of the sample population had chest pain explicitly specified on their referral letters for CTPA (Table 5.2). Similarly, previous history of PE was recorded for a limited number of patients. In contrast, over a third of the sample population had elevated D-dimer levels indicated on their CTPA referral letters. Approximately one fifth of the sample population was COVID-19-positive patients, of whom most were hospitalised. Of the hospitalised patients, a small number required ventilation.

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Table 5.2 Number of patients for the different levels of clinical indicators

Patient clinical indicator	Number of patients presenting with the clinical indicator (%)	Number of patients presenting without the clinical indicator (%)	Total number of patients
Chest pain	47 (3.9)	1172 (96.1)	1 219
Increased D-dimer level	437 (35.8)	782 (64.2)	1 219
Previous history of PE	70 (5.7)	1149 (94.3)	1 219
COVID-19 positive	33 (20.9)	125 (79.9)	158
Post 10 days COVID-19 test	81 (51.3)	77 (48.7)	158
COVID-19 outpatient	15 (9.5)	143 (90.5)	158
COVID-19 hospitalised patient	110 (69.6)	48 (30.4)	158
COVID-19 ventilated patient	3 (1.9)	155 (98.1)	158

5.5 Relation between elevated D-dimer levels and positive PE

The sample population of 1 219 patients was analysed to establish if a relation existed between elevated D-dimer levels and a positive diagnosis of PE with CTPA. This relation was analysed in terms of the sample population (n = 1 219) and its subpopulations. One of the subpopulations was a population that excluded COVID-19-referred patients (n = 955). Another subpopulation comprised patients with prehistory of PE (n = 106), which excluded patients referred because of COVID-19. The relation between elevated D-dimer levels and a positive diagnosis of PE was also analysed for the subpopulation of COVID-19 referral patients (n = 158). Because radiologists also reported on several ancillary clinical findings during CTPA, these findings were also reported.

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5.5.1 Sample population

After a CTPA had been performed, the sample population of 1 219 patients yielded a small number of patients with PE. After scrutinising the proportion of PE-positive patients in the clinical indicator combination groups, no specific trends in the relation between elevated D-dimer levels and a positive PE diagnosis could be identified. However, a goodness of fit chi-square test revealed that the number of male patients (n = 85) diagnosed with PE was significantly less than the female patients (n = 119) at $\alpha = .05$ (χ^2 (1, N = 204) = 5.67, p <.017). In this population, 16.7% of the patients were diagnosed with PE after CTPA (Figure 5.2). Furthermore, all four clinical indicator groups were represented by patients who had received a positive PE diagnosis following a CTPA. The proportion of patients diagnosed with PE in the small clinical indicator combination group of patients with chest pain and negative D-dimer tests (n = 59) exceeded 50% when they were compared to the other groups. In contrast, the proportion of patients diagnosed with PE in the other three groups was less than 20%.

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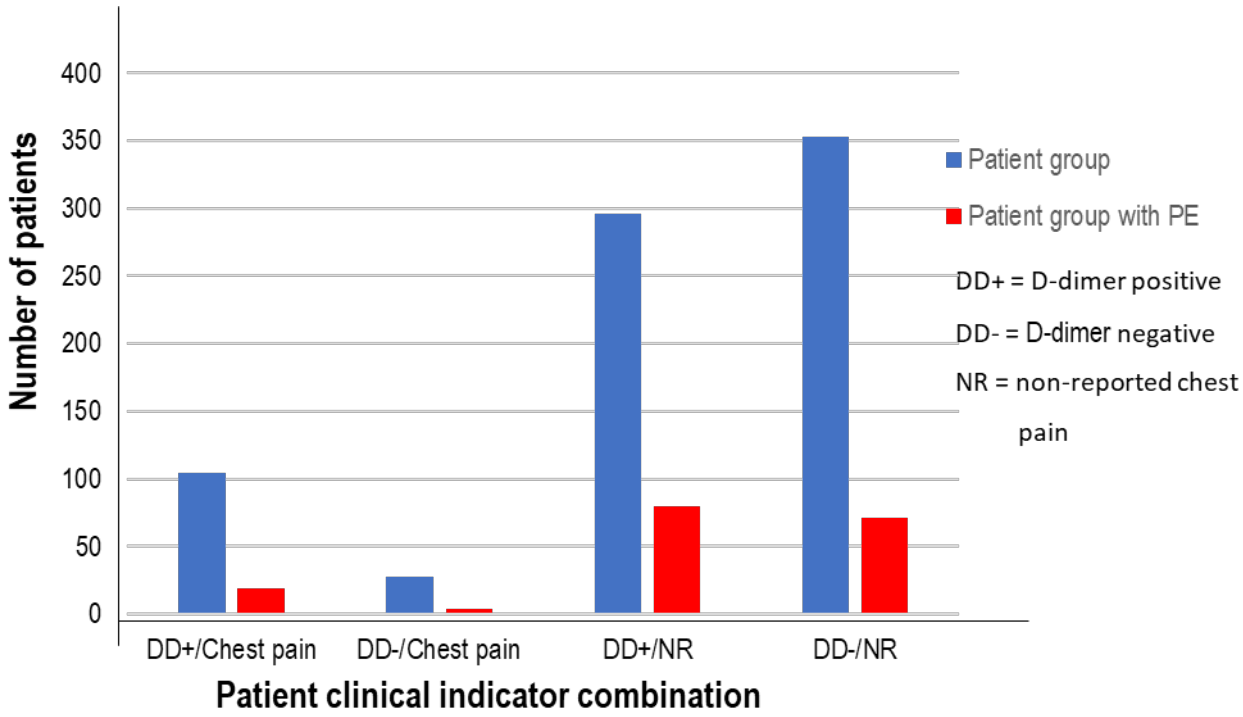

Figure 5.2 PE occurrence in different patient clinical indicator combination groups of the sample population

A chi-square test of independence was performed to establish if different patient groups, classified in terms of different combinations of clinical indicators, with positive or negative PE diagnosis, were related. The test revealed significant results at α = .05 (χ^2 (3, N = 1 219) = 58.85, p < .0001). Table 5.3 provides a contingency table of the chi-square test showing the different clinical indicator groups and PE diagnosis.

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Table 5.3 Contingency table of chi-square test results for the sample population

	PE diagnosis		
Patient clinical indicator combination group	**PE positive**	**PE negative**	**Row totals**
Chest pain + D-dimer positive	23 (24.43) [0.08]	123 (121.57) [0.02]	146
Chest pain+ D-dimer negative	31 (9.87) [45.20]	28 (49.13) [9.09]	59
Non-specified + D-dimer positive	60 (76.65) [3.62]	398 (381.35) [0.73]	458
Non-specified + D-dimer negative	90 (93.05) [0.10]	466 (462.95) [0.02]	556
Column totals	204	1 015	
TOTAL			**1 219**

5.5.2 Subpopulation excluding COVID-19 referrals and patients with a prehistory of PE

The proportions of PE in the different clinical indicator combination groups were similar to that of the sample population. As anticipated, patients with PE diagnosis after CTPA were recorded for all four clinical indicator groups in this subpopulation (n = 995). After forming this subpopulation by excluding COVID-19 patients and patients with a previous history of PE, no specific trends in the relation between elevated D-dimer levels and a positive PE diagnosis could be established. Figure 5.3 shows the proportions of positive PE diagnosis patients in the different clinical indicator combination groups.

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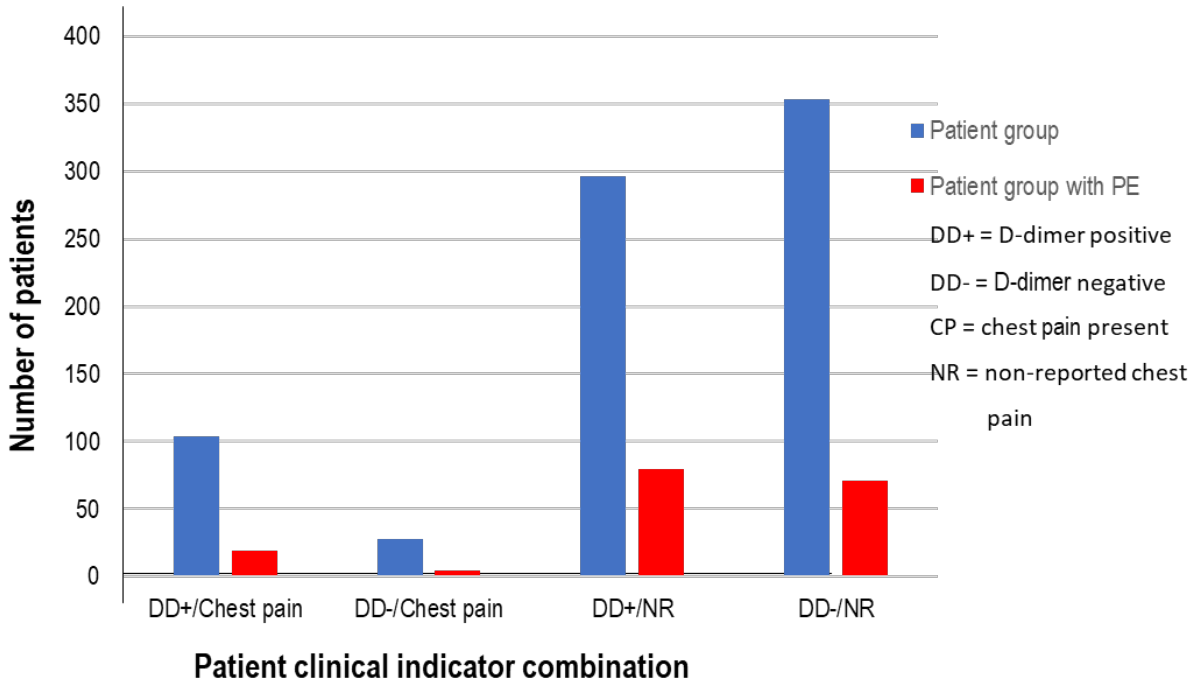

Figure 5.3 PE occurrence in different patient clinical indicator combination groups in the subpopulation, excluding COVID-19 referrals and patients with PE prehistory

A chi-square test of independence was performed on the different clinical indicator groups to establish if the groups were independent or not. To satisfy the assumptions of the test, the test was performed using a 2 × 2 contingency table with the two categories of D-dimer levels and the two categories of PE. The outcome of the test was not significant at $\alpha = .05$ (χ^2 (1, N = 995) = 1.84, p = .175). Table 5.4 shows the contingency table of the chi-square test for the subpopulation, which comprises the sample population excluding the COVID-19 referrals and patients with PE prehistory.

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Table 5.4 Contingency table of chi-square test results for the sample population excluding COVID-19 referrals and patients with PE prehistory

	PE diagnosis		
Patient clinical indicator combination group	**PE positive**	**PE negative**	**Row total**
D-dimer positive	75 (83.08) [0.79]	99 (90.92) [0.72]	174
D-dimer negative	381 (372.92) [0.18]	400 (408.08) [0.16]	781
	456	499	
TOTAL			**955**

5.5.3 Subpopulation of patients with a prehistory of PE

Within the subpopulation of patients with prehistory of PE (n = 106), excluding COVID-19 patients, the number of patients with a positive diagnosis of PE after a CTPA for each clinical indication combination group was relatively small. The proportion of PE-positive diagnoses of the two D-dimer groups who had reported chest pain was less than 10%: 8% for D-dimer negative group and 7% for the D-dimer positive indicator groups (Figure 5.4). For the two D-dimer groups with no reported chest pain, combined, the proportions of PE-positive diagnoses were 11% for D-dimer negative group and 17% for the D-dimer positive group.

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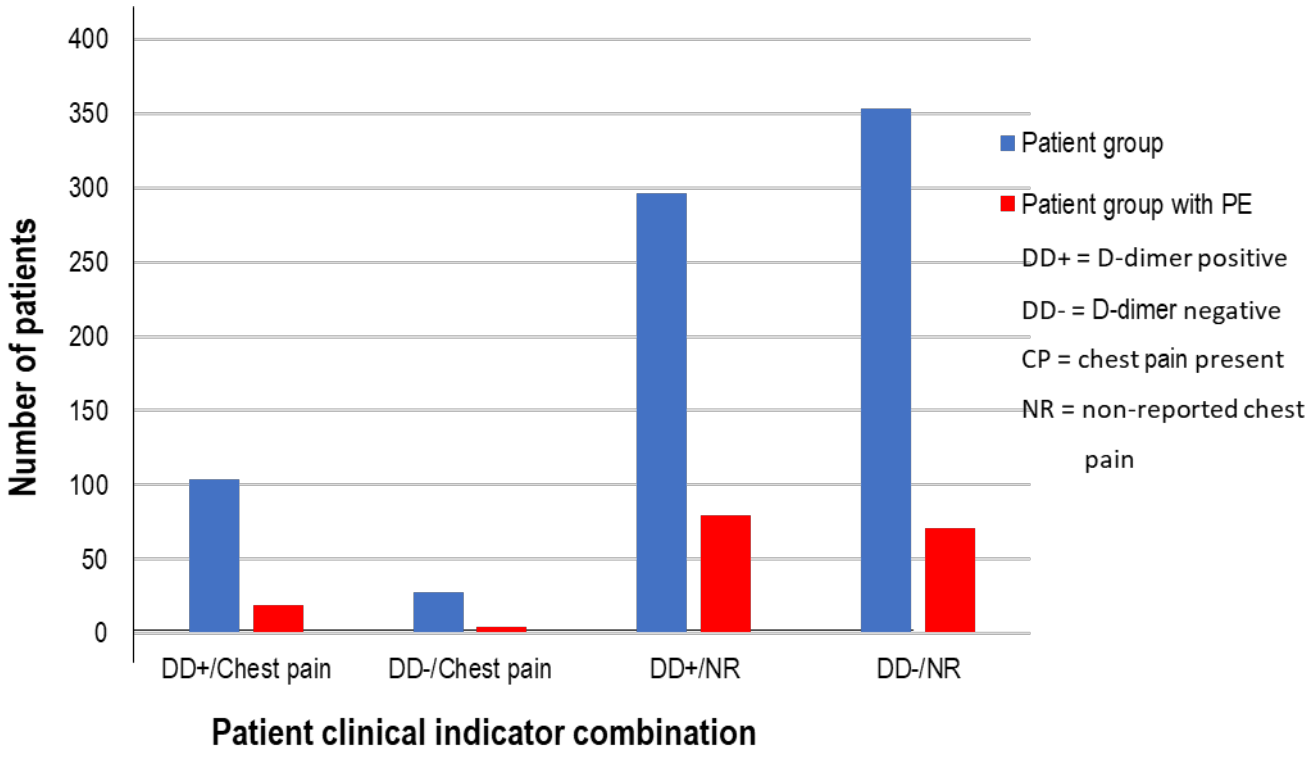

Figure 5.4 **PE occurrence in different patient clinical indicator combination groups in the subpopulation excluding COVID-19 referrals and patients with PE prehistory**

5.5.4 Subpopulation of COVID-19 referral patients

Similar, to the other subpopulations of patients (n = 158), the proportions of COVID-19 referral patients with a positive yield of PE after CTPA were also relatively small for each clinical indication combination group. The proportions of PE-positive diagnoses ranged from 8 to 19% for the four clinical groups (Figure 5.5). For the two COVID-19-positive combination groups, 10% of the patients were PE positive in the D-dimer positive group and 8% in the D-dimer negative group. The proportions of PE-positive patients were marginally greater for the other two groups: 13% for the D-dimer positive group and 19% for the D-dimer negative group.

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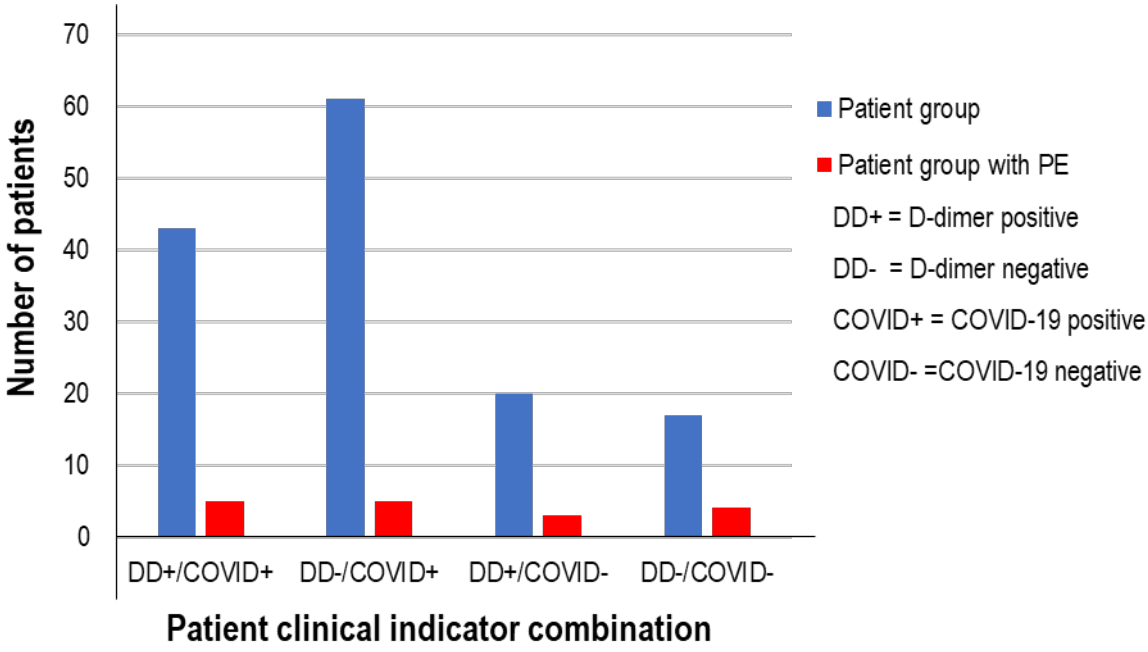

Figure 5.5 PE occurrence in different patient clinical indicator combination groups in the subpopulation of COVID-19 referral patients

When viewing the data gathered from the PACS of COVID-19 referral patients, few patients had reported chest pain and had a prehistory of PE. Of the 158 COVID-19 referral patients, 7% had a prehistory of a PE diagnosis, of which most were COVID-19 positive (Table 5.5). It was also noted that seven patients who were COVID-19 positive (D-dimer negative and PE negative) had a prehistory of PE and also presented with chest pain.

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Table 5.5 Number of patients with prehistory of PE and/or chest pain within different clinical indicator combination groups

Patient clinical indicator combination group	Number of patients within combinations of clinical indicator group	Number of patients with prehistory of PE	Number of patients with chest pain
D-dimer positive + COVID positive + PE positive	5	1	1
D-dimer positive + COVID negative + PE positive	3		1
D-dimer positive + COVID positive + PE negative	43	2	4
D-dimer positive + COVID negative + PE negative	20		2
D-dimer negative + COVID positive + PE positive	5		3
D-dimer negative + COVID negative + PE positive	4		1
D-dimer negative + COVID negative + PE negative	17	1	2
D-dimer negative + COVID positive + PE negative	61	7	10
TOTAL	**158**	**11**	**24**

To establish if the groups were independent or not, a chi-square test of independence was performed on the different clinical indicator groups. The test was performed using a 2 × 2 contingency table to satisfy the assumptions of the test (Table 5.6). The test used the proportions of patients with PE-positive diagnoses in the D-dimer levels grouped with C0VID-19-positive patients (n = 114). The test revealed that the groups were independent with non-significant test outcomes (χ^2 (1, N = 114) = 0.28, p = .597).

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Table 5.6 Contingency table of chi-square test results of the subpopulation consisting of the COVID-19 referral patients

	PE diagnosis		
Patient clinical indicator combination group	**PE positive**	**PE negative**	**Row total**
D-dimer negative + COVID positive	5 (5.79) [0.11]	61 (60.21) [0.01]	66
D-dimer positive + COVID positive	5 (4.21) [0.15]	43 (43.79) [0.01]	48
Column total	10	104	
TOTAL			**114**

5.5.5 Ancillary clinical findings during CTPA

During the CTPA, the radiologists reported on several ancillary clinical findings. In this study of more than a thousand patients, the radiologists reported 11 different types of ancillary abnormalities, of which more than one occurred in several patients (Table 5.7). The most prevalent of these abnormalities were visualised bone abnormalities, which included osteopenia, bone metastases and osteoarthritis. The second most prevalent ancillary finding was the presence of pleural effusion on the CTPA. In a few instances, thyroid abnormalities and masses were also detected. A positive PE diagnosis was found to be the highest in the pulmonary hypertension ancillary finding group, whereas the second most frequent positive PE diagnosis was found for the heart abnormality ancillary group.

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Table 5.7 Number of patients with ancillary clinical findings and number of patients with PE diagnosis per clinical finding

Ancillary clinical finding	Number of patients (%)	Number of patients with positive PE (%)
Pulmonary hypertension	195 (16.0)	58 (29.7)
Pleural effusion	233 (19.1)	48 (19.7)
Nodules	100 (8.2)	9 (9.0)
Masses	35 (2.9)	2 (5.7)
Ground glass opacification	187 (15.3)	34 (18.2)
Lymphadenopathy	162 (13.3)	20 (12.3)
Heart abnormalities	110 (9.0)	23 (20.9)
Pulmonary vascular abnormality	62 (5.1)	9 (14.5)
Thyroid abnormalities	16 (1.3)	3 (18.8)
Visualised abdominal abnormalities	191 (15.7)	24 (12.6)
Visualised bone abnormalities	389 (31.9)	64 (16.5)

5.6 Comparative analysis of sample population and subpopulations

A comparative analysis of the sample population and subpopulations was undertaken to establish the relation between elevated D-dimer levels in the blood and a positive PE diagnosis with CTPA. This comparison revealed that the percentage of patients with elevated D-dimer levels in the three subpopulations was relatively low, ranging from approximately 11 to 19% of the patients (Table 5.8). A chi-square test of independence revealed no differences between the number of patients with positive PE in the elevated D-dimer subgroups of the three populations. However, when inspecting the patients with a positive PE diagnosis in the three populations, the comparison revealed that the percentage of patients with elevated D-dimer levels ranged from approximately 55 to 59% of the

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patients. Similarly, the chi-square test of independence showed that the number of patients with elevated D-dimers in the patients' subgroup of positive PE diagnosis did not differ $\alpha = .05$ (χ^2 (2, N = 618) = 0.022, p = .99).

Table 5.8 Comparative analysis of the different patient groups

Population	Population size	Elevated D-dimer patient group		Positive PE patient group	
		Number of patients with elevated D-dimer levels	Number of patients with elevated D-dimer levels with a positive PE (%)	Number of patients positive PE	Number of patients within the PE group with elevated D-dimer levels (%)
Sample	1 219	604	114 (18.7)	204	114 (55.9)
Subpopulation (excluding COVID+ and prehistory of PE)	955	499	75 (15.0)	174	99 (56.9)
Subpopulation COVID +	158	71	8 (11.3)	17	10 (58.8)

5.7 Discussion

After analysing the sample population of 1 219 patients and several subpopulations, the results did not indicate a strong relation between elevated D-dimer levels and a positive PE diagnosis with CTPA. Overall, relatively few patients in the sample population of this study had a positive diagnosis of PE – only 16.7%. Of these patients, approximately 50% had elevated D-dimer levels, which was also true for the subpopulation excluding COVID-19 referral patients. In contrast, a few patients (less than 20%) of the subgroup with elevated D-dimer levels had a positive diagnosis of PE. These results show that, although approximately half the patients diagnosed with PE had elevated D-dimer

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levels, only a few patients with elevated D-dimer levels had been diagnosed with PE, which indicates that the relation between elevated D-dimer levels and a positive yield of PE after CTPA was weak. This outcome substantially impacts the understanding of which diagnostic tests should be used when deciding to perform a CTPA and could contribute to the reduction in the use of radiation.

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Chapter 6

Discussion and Concluding Remarks

6.1 Introduction

The relatively common pulmonary embolism (PE) disease could present a patient with life-threatening complications. In acute cases, PE may be fatal (Al-Rammah et al., 2016). In radiology practices, the gold standard for PE diagnosis is through using the highly specific and sensitive imaging procedure of computed tomography pulmonary angiography (CTPA) (Pathak et al., 2011; Youssf et al., 2014; Doğan et al., 2015). When patients show elevated D-dimer levels in the blood, it is standard practice that these patients are also referred for CTPA to rule out PE (Van Belle et al., 2006). However, PE is not always confirmed in these referred patients, and this begs the question of whether patients with elevated D-dimer levels should be routinely referred for CTPA and face the risk of the radiation dose and contrast media (CM) administration associated with CTPA imaging (Alshumrani et al., 2021). An understanding of the relation between elevated D-dimer levels in the blood and a positive PE diagnosis with CTPA may influence current referral practices for patients with elevated D-dimer levels.

6.2 Pulmonary embolism

The sensitivity and specificity of CT as a diagnostic modality have led to the routine use worldwide of CTPA in hospitals and private radiology practices to diagnose PE in patients. Consequently, growing evidence suggests overuse of CTPA (Salehi et al., 2021). This increased use of CTPA, especially in the emergency department, has brought about concerns about radiation and adverse reactions to CM in patients (Sun & Lei, 2017; Kara et al., 2018; Al-Zaher et al., 2020). This retrospective South African study, conducted in a single private radiology practice in Bloemfontein, revealed that less

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than 20% (16.7%) of more than 1 000 patients were positively diagnosed with PE after CTPA. This positive yield of PE falls within the lower end of the suggested acceptable range (15.4%–34.7%) as described by The Royal College of Radiologists (UK) (Vrettos et al., 2017). A similar result was found by a study conducted in two hospitals in the United Kingdom, where the positive yield of PE was 14% in 236 CTPA scans. In contrast, in North America, the positive yield of PE specifically in emergency departments is only 8% (De Wit et al., 2022). However, this study, at the private radiology practice in Bloemfontein, revealed that more female patients were diagnosed with PE than male patients, in contrast to the study by Turetz et al. (2018), who found that PE was more prevalent in male than female patients.

6.3 Relation between elevated D-dimer levels and PE

The possible fatal risks associated with PE and the costs of monitoring necessitate the timeous and effective diagnosis of PE. Today, D-dimer laboratory assays are extensively used in hospitals and private practices to identify PE risk, because elevated D-dimers indicate thrombus formation (Weitz et al., 2017; De Wit et al., 2022). Patients with positive D-dimer tests are usually referred for CTPA for evaluation of PE (Van Belle et al., 2006). However, elevated D-dimers are not only indicative of PE, but also of sepsis, malignancy, pregnancy, myocardial infarction, or recent surgery (Righini et al., 2014), and more recently, COVID-19 (Yong et al., 2020; Masselli et al., 2021). The association of elevated D-dimer levels with several clinical conditions could be a contributing factor to the increased use of CTPA to exclude PE. This notion is supported by a study that was published by Kubak et al. in 2016, who found a positive yield of 26.3% of PE after CTPA examinations of 822 patients with elevated D-dimer levels, using a higher threshold value. A further contributor to the relatively low yield of positive PE after CTPA could be physicians who seldom use decision rules after D-dimer testing, because of their complexity and credibility (De Wit et al., 2022). In this study, at the private radiology practice in Bloemfontein, 83 of the 604 patients (13.7%) with elevated D-dimer levels were diagnosed with PE

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after CTPA. Similarly, in the COVID-19 patient group, 10.4% of patients with elevated D-dimers had a positive PE diagnosis. The outcome of this study, therefore, supports the notion that a strong relation between elevated D-dimer levels and a positive PE yield could not be established.

6.4 Concluding remarks and recommendations

From this study, it can be concluded that there is not a strong relation between elevated D-dimer levels in the blood and a positive yield of PE after CTPA. Although CTPA is an invaluable tool in the diagnostic work-up and management of patients with suspected PE, the routine use of CTPA for all patients with elevated D-dimer levels at this private practice raises concerns. CT as an imaging modality comes with a burden of high radiation dose and the potential for adverse effects from the administration of CM. This finding necessitates further investigation into the required routine best practices when deciding which patients should be referred for CTPA during the routine PE workup. In particular, clinical decision rules for PE workups need refining, especially to limit unnecessary CTPA referrals. The findings of this study may result in the revision of PE workups in the private practice and also assist with the development of practice guidelines to, ultimately, improve the quality of service.

The radiation dose and the administering of CM at a private radiology practice for patients who underwent CTPA examinations were assessed with the use of a DCI tool. However, the DCI results indicated shortcomings in the current standard of practice. The high number of CTPA requests, despite the low percentage of positive PE diagnoses, was the most significant flaw found. Based on the study's findings, it is suggested that the standard practice protocols should include an explanation of the CTPA procedure, benefits, radiation exposure risks, and CM and should be distributed to all referring physicians. Dose reduction techniques should be employed, such as a helical high-pitch acquisition technique; CTPA images will still be rendered of excellent diagnostic quality whilst using an ultra-low dose of iodinated contrast and low radiation dose (Rajiah et al., 2019). A study by Aldosari and Sun

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(2019) confirmed that double low-dose CTPA is feasible for diagnosing PE and provides significant reductions in radiation and CM doses without compromising diagnostic image quality. Another dose optimisation technique that can be employed is a low kV technique combined with high iterative reconstruction parameters for CTPA (Bellizzi et al., 2023). Furthermore, Chen et al. (2017) indicates that using lower doses of iodine contrast is feasible without it resulting in suboptimally opacified CTPA scans. It is, therefore, recommended that private practices use these recommendations to build the capacity of health care practitioners regarding radiation exposure safety and CM effects and to provide quality health care services to patients.

Additionally, it is advised that supplementary information is added to the training curriculum of the diagnostic radiography course. The strength of this study lies in the development of a novel DCI. The DCI could be used as a template in replication studies (nationally and internationally) or future studies on the relation between elevated D-dimer levels and a positive CTPA to confirm pulmonary emboli. In addition, the DCI can be used as a supporting decision-making tool in the healthcare industry and may be of use in government and private practices in South Africa and abroad.

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Appendices

Appendix A: Ethical approval letter HSREC

UNIVERSITY OF THE FREE STATE
UNIVERSITEIT VAN DIE VRYSTAAT
YUNIVESITHI YA FREISTATA

UFS·UV
HEALTH SCIENCES
GESONDHEIDSWETENSKAPPE

Health Sciences Research Ethics Committee

17-Sep-2021

Dear **Mrs Rochelle Kruger**

Ethics Clearance: **THE RELATION BETWEEN ELEVATED D-DIMER LEVELS AND A POSITIVE COMPUTED TOMOGRAPHY PULMONARY ANGIOGRAM TO CONFIRM PULMONARY EMBOLI: A RETROSPECTIVE STUDY**

Principal Investigator: **Mrs Rochelle Kruger**

Department: **Radiography - CUT**

Submission Page

APPLICATION APPROVED

Please ensure that you read the whole document

With reference to your application for ethical clearance with the Faculty of Health Sciences, I am pleased to inform you on behalf of the Health Sciences Research Ethics Committee that you have been granted ethical clearance for your project.

Your ethical clearance number, to be used in all correspondence is:**UFS-HSD2021/1235/2809**

The ethical clearance number is valid for research conducted for one year from issuance. Should you require more time to complete this research, please apply for an extension.

We request that any changes that may take place during the course of your research project be submitted to the HSREC for approval to ensure we are kept up to date with your progress and any ethical implications that may arise. This includes any serious adverse events and/or termination of the study.

A progress report should be submitted within one year of approval, and annually for long term studies. A final report should be submitted at the completion of the study.

Research conducted in any Department of Health facility: Researchers are required to sign and return the HSREC approval letters to the provincial Department of Health where they applied. It is also a requirement for researchers to submit electronic copies of their final research findings, and/or make a presentation of their findings and recommendations at departmental research days when and where indicated.

The HSREC functions in compliance with, but not limited to, the following documents and guidelines: The SA National Health Act. No. 61 of 2003; Ethics in Health Research: Principles, Structures and Processes (2015); SA GCP(2006); Declaration of Helsinki; The Belmont Report; The US Office of Human Research Protections 45 CFR 461 (for non-exempt research with human participants conducted or supported by the US Department of Health and Human Services- (HHS), 21 CFR 50, 21 CFR 56; CIOMS; ICH-GCP-E6 Sections 1-4; International Council for Harmonisation (ICH) Harmonised Guideline, Integrated Addendum to ICH E6(R1), Guideline for Good Clinical Practice (GCP) E6(R2), 2016, SAHPRA Guidelines as well as Laws and Regulations with regard to the Control of Medicines, Constitution of the HSREC of the Faculty of Health Sciences.

For any questions or concerns, please feel free to contact HSREC Administration: 051-4017794/5 or email EthicsFHS@ufs.ac.za.

Thank you for submitting this proposal for ethical clearance and we wish you every success with your research.

Yours Sincerely

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Appendix B: Permission to conduct a research study at the radiology practice

[redacted]

DIAGNOSTIESE RADIOLOË • DIAGNOSTIC RADIOLOGISTS

[redacted]

23 February 2021

MS ROCHELLE KRUGER
PO BOX 11105
UNIVERSITAS
BLOEMFONTEIN
9301

Dear Rochelle

REQUEST RESEARCH STUDY:

Your request to conduct a research study "THE EFFECTIVENESS OF ELEVATED D-DIMER TEST AS A PREDICTOR OF A POSITIVE COMPUTED TOMOGRAPHY PULMONARY ANGIOGRAM FOR PATIENTS WITH CHEST PAIN AND SUSPECTED PULMONARY EMBOLISM]", at [redacted] Inc, has been approved.

Kind Regards

[redacted]

PRACTICE MANAGER

[redacted]

Appendix C: Cost of CTPA examination

[redacted]

BLOEMFONTEIN [redacted] STREET, BLOEMFONTEIN, 9301

TEL: (051) 400 7040/30/33/43/47 FAX: (051) 4443622

Medical Aid Details	PVM	Branch	P.E.R.O.	Statement Date
		[redacted]	3863724	2021/01/11

[redacted]

TERMS OF PAYMENT
Strictly cash
Interest will be charged on overdue accounts

Administrative errors do occur. Please contact our accounts department should you have any queries on this account

Patient's Name			DOB	
Employer's Name			Member no	

Date	Details	Tariff	Amount
11 Jan 2021	CT CHEST FOR PULMONARY EMBOLISM	30880	R 9 332.30
11 Jan 2021	SCANLUX 300 100ML 723020001	30880	R 426.73
11 Jan 2021	JELCO 20G PINK 15053/001	30000	R 19.15
11 Jan 2021	WEBCOL 426125004	30000	R 0.37
11 Jan 2021	SALINE 100CML 0,9% 747974018	30000	R 1.16
11 Jan 2021	CONTRAST PUMP TUBE X291036001	30000	R 261.98
11 Jan 2021	PATIENT TUBE XD2000 259807031	30000	R 143.60

This quotation is only valid for this specific examination, and for a period of 7 days. It is an estimated cost, subject to change, if contrast or other materials are required.

Referring Doctor		Balance Owing	R 9 185.55

[redacted]

PLEASE QUOTE THIS REF NO. FOR PAYMENT AND OTHER ENQUIRIES ON THIS STATEMENT. ➡ REF NO. 467

Appendix D: Data capturing instrument

Anonymised Patient Code:

Data capturing instrument of CT PE					1	2	3	4
Health institution:	Private Participating Radiology Practice							
Name of machine:	GE LIGHT SPEED							
Model of machine:	Light Speed VCT							
The number of detector rows:	Single source (64)							
Daily QC of CT scanner performed:	YES		NO					
Patient examination number:								
AGE:								
WEIGHT:	< 100 kg		> 100 kg					
GENDER:	FEMALE		MALE					
CT protocol used:	CT Chest for PE							
CLINICAL INDICATION								
Chest Pain	YES		NO					
Increased D-dimer	YES		NO					
Previous history of PE	YES		NO					
COVID-19								
POSITIVE	YES		NO					
NEGATIVE	YES		NO					
POST 10 DAYS	YES		NO					
Out-patient	YES		NO					
Hospital patient	YES		NO					
Ventilated patient	YES		NO					
PARAMETERS								
Scanning Mode: Helical								

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IV contrast used:								
Scanlux 370	YES		NO					
Scanlux 370 volume used for an exam:								
Imeron 400	YES		NO					
Imeron 400 volume used for exam:								
Tube Voltage (kVp):	120 kVp							
Scan Dose Reduction Percentage:	30%							
Tube current modulation:	0n (modulation transfer function)							
Auto mA quality factors (e.g. nose index, mAs/slice):	Nosie: 25							
	mAs/slice: Smart mA							
Scan time:								
Scan length in mm:	**Start:**							
	End:							
Rotation time in seconds:	0,6 - 0,7 s							
Pitch & Speed:	0,984:139,37							
Beam collimation:	64 x 0,625 mm							
The number of scan phases:								
1 (Scout)								
2 (Pulmonary artery location)								
3 (Bolus timing)								
4 (Pulmonary angiogram)								
5 (Expiration chest)								
6 (Other)								
Scan field of view:								
Slice thickness in mm:	0,625 mm							
Scan range (mm):	Body 32 mm							
CTDI volume (mGy):								
DPL (mGy-cm):								

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Total exam DLP (mGy-cm):								
Reporting template:								
Positive	YES		NO					
Negative	YES		NO					
Additional clinical findings:								
Pulmonary hypertension	YES		NO					
Pleural effusion	YES		NO					
Nodules	YES		NO					
Mass	YES		NO					
Ground-glass opacification	YES		NO					
Lymphadenopathy	YES		NO					
Clinical abnormalities:								
Heart	YES		NO					
Vasculature	YES		NO					
Thyroid	YES		NO					
Visualised abdomen	YES		NO					
Visualised bone	YES		NO					

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Appendix E: GE Light Speed Quality Assurance Certificate

imagination at work

GE Healthcare Technologies

Unit 2, 130 Gazelle Avenue
Corporate Park, Midrand, 1685
Private Bag X124
Halfway House, 1685
Tel: 27-11-653 8800
Fax: 27-11-653 8801
QA Technical Manager; Coloman Hendrik

GE LIGHT SPEED VCT
QUALITY ASSURANCE
Bloemfontein [redacted]

Pass

License No; 4231-28
Machine no;28
ZA Number: ZA1000CT03
Ref No;ZA1000CT03
Unit Serial Number: 88747WG1
Date QA Done: 19-09-2013
Customer contact persone; [redacted]
Tel; [redacted]
Fax; [redacted]

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Appendix F: DOH Inspection Body Certificate of Conformance

INDEX TESTING

P.O. Box 5122, Bracken Gardens, 1452
Ph – 083 600 2653 Fax – 011-867 2050 e-mail – gail.paton@absamail.co.za
Abraham Wessels – 083 268 9470; email– abe@y2000med.co.za

sanas

QC INSPECTION - CT UNIT

Inspection and tests done by Mr Abraham Wessels, C.T. and 'Safety of Premises' signatory for Index Testing.

Customer Particulars	**Date of Inspection:** 31 August 2023
Licensee [redacted]	**Date of Report:** 01 September 2023
Physical Address: [redacted] Bloemfontein, Free State, South Africa	
Postal address: P.O. Box 12044 Brandhof 9324	**Department:** X-ray Department **Room:** CT Room
Phone: [redacted]	**Appointed person responsible for QC Test:**
Email: [redacted]	[redacted]

A UNIT PARTICULARS	
Date of Installation: 13-08-2013	
DoH Licence no: 4231/28	
Tube Ser. no: 231527Gi3	Testing Tech: A. Wessels
Date of replacement/ upgrade: 20-08-2021	Type of Tests: (Annual QC /Acceptance/Post Repairs)
Operator's Manual: On Site	Annual QC
Unit labelled with make, model, serial & licence no Yes	Inspection no Number 1 of 2023 File Name: QC517 31-08-2023
Warning sign Yes	Warning Light All working

B COMPONENT PARTICULARS			
UNIT	**MAKE**	**MODEL**	**SERIAL NUMBER/ ID NUMBER**
Computed Tomography	GENERAL ELECTRIC	LIGHTSPEED VCT	88747WG1/ 9543YC0 ZA1000CT03

TESTING EQUIPMENT DETAILS

Testing Tech	**A Wessels**		
Equipment make	**Model**	**S/n**	**Calibration date**
Unfors Xi	Base unit Platinum	164866	22-04-2021
Unfors Xi	CT Detector	165145	22-04-2021
Unfors Xi	Light Detector	261759	22-04-2021
Inovision	451-P	6045	02-09-2019

Index Testing is licensed in terms of section 4(1) (b) of the Hazardous Substances Act, 1973 (act 15 of 1973) by SAHPRA, Directorate Radiation Control to perform maintenance tests.
Licence Number: 1004 **SANAS (ISO 17020) accreditation no: XRAY0004**

Testing Methodology: 'CT, Version 2, amended October 2012'
Testing according to SAHPRA Diagnostic QC licensing conditions (29 August 2022).

GPaton

Gail Paton
Technical & Quality Manager

Abraham Wessels
CT Field Service Engineer

Abraham Albertus Cilliers Wessels
Abraham Albertus Cilliers Wessels

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INDEX TESTING

sanas

Report Summary and Results Check of Sub-annuals performed

III.1.8. Image Display Monitor & Reporting Monitor			Done/Comment
29a	Condition of Image Display Monitor	On acceptance & At least 6 monthly.	Checked/ Good
29b	Condition of Reporting Monitor – Each reporting monitor must be labelled —" REPORTING MONITOR"	On acceptance & as required or at least weekly	Checked/ Good
31	Distance and angle calibration ± 5 mm± 3° (degrees)	On acceptance & 3 Monthly	CT Monitor used as Display Only
32	Reporting monitors – Resolution	On acceptance & 3 Monthly	CT Monitor used as Display Only

Check of Sub-annuals performed

III.1.12. Computed Tomography			Done/Comment
46	Indicators, radiation warning lights at entrance, medical and other safety checks	On acceptance & Daily	Checked
47	Image Noise	On acceptance & Daily	Done
48	CT number values	On acceptance & Daily	Done
49	Scan plane localization from alignment lights	On acceptance & 3 Monthly	Done

Results of tests done: Safety of premises

III.2.1. General Tests				Date of Test	Pass/Fail
75	Safety of premises	On acceptance, when the workload increases or technique factors change that may jeopardise premises safely	Controlled areas 5mSv/year. Uncontrolled areas 1mSv/year	13-08-2013	PASS

Results of tests done: Annual QC

III.2.6. Reporting Monitor				Pass/ Fail	Comments
119	Dicom Greyscale Calibration	On acceptance & 12 monthly	GSDF +-10%	n/a	Used as display only
119.1	Minimum requirements for Monitors	On acceptance & 12 monthly	Comply Table 4	n/a	Used as display only
119.2	Reporting Monitors – Greyscale (Luminance response)	On acceptance & 12 monthly	Ratio to Black ≥ 250	n/a	Used as display only
120	Luminance Uniformity	On acceptance & 12 monthly	Maximum variation ≤ 30%	n/a	Used as display only
121	Variation between Monitors	On acceptance & 12 monthly	≤ 30%	n/a	Used as display only
122	Room Illumination	On acceptance & 12 monthly	≤ 15 Lux for CRT displays & < 20 Lux for LCD displays	n/a	Used as display only

Results of tests done: Annual QC

III.2.8. Computed Tomography				Pass/Fail
140	Image Noise	On acceptance & 12 monthly	Baseline ± 10% Inter-slice variation; Mean ± 10%	PASS
141	CT number values	On acceptance & 12 monthly	Water baseline ± 5HU. Other material: baseline ± 10HU	PASS
142	CT number uniformity	On acceptance & 12 monthly	Head phantom: ≤ ± 10HU Body phantom: ≤ ± 20HU	PASS
143	High contrast spatial resolution	On acceptance & 12 monthly	Baseline ± 20%	PASS
144	Computed Tomography dose index (CTDI)	On acceptance & 12 monthly	Baseline ± 15%	PASS
145	Image slice thickness	On acceptance & 12 monthly	Baseline ± 20% or ± 1mm, whichever is greater	PASS
146	$CTDI_{vol}$ for single slice rotation	13/12 after installation & 3 yearly	≤ Reference dose	PASS

Results of tests done: Annual QC

III.2.15.3. Computed Tomography		Scan Factors	Result (mGy-cm)
262	Adult Head (Standard Brain)	120kV/196mA/SD=4.1~/Head/2.5000mm/8i/Tilt S3.5/rot speed=1.0sec/Axial	92.14
263	Adult Chest	120kV/268mA/SD= 25.4~/Large Body/0.625mm/Speed=39.38/pitch=0.984:1/rot speed=0.7sec/He+	9.86
264	Adult abdomen-pelvis	120kV/135mA/SD=25.0~/Large Body/0.625mm/Speed=55.00/pitch=1.375:1/rot speed=0.6sec/He+	165.97
265	IVP	120kV/135mA/SD=25.0~/Large Body/0.625mm/Speed=55.00/pitch=1.375:1/rot speed=0.6sec/He+	165.97
266	Paediatric abdomen	100kV/72mA/Ped Body/2.500mm/Speed=39.38/pitch=0.984:1/rot speed=0.4sec/He+	1.17
267	Paediatric Head	120kV/173mA/Head/SD=4.1~/2.500mm/8i/rot speed=1.0sec/Axial	17.82

NOTE:

Licence/Unit no.	Date Tested	Tested By:	Technical Signatory - A Wessels	Technical & Quality Manager G Paton
4231/28	31-08-2023	A. Wessels		G Paton

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INDEX TESTING

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Quality Assurance Raw Data

Date: 31 August 2023

Worksheet #1

Phantom: Q/A Phantom (Model 2144715 Rev 6>PMMA< s/n 1002647)

RAW DATA Collected at site					
TEST no. 140 & 142 Noise and CT No. Uniformity					
Noise (ROI 20mm box)					
	Spec				
	Mean CT#	**STD. DEV**	**Mean CT#**	**STD. DEV**	**Uniformity diff.**
ROI CTR	0 ±3	4.6 ± 0.6 HU	-0.52	4.73	1.298
Edge Top			0.46	3.22	
Edge left			0.27	3.62	
Edge Right			-0.01	3.32	
Edge Bottom			-0.27	3.57	
CT # Uniformity - 0 ±3 HU					
120kV/135mA/5.000mm/Speed=10.62/ Pitch=0.531:1/Rot Speed=0.1S/He+					

Worksheet #2

Phantom: Φ240 water Scan conditions: 120kV/260mA/5mmx4/2-stack/S area/1,5 sec/FC 70/5mm

TEST no. 141 CT Number Value and TEST no 143 High Contrast Spatial resolution							
Date	**Contrast Scale**			**High Contrast Spatial & MTF**			**Align Yes/No**
		Mean CT#	STD. DEV				
31/08/2023	**Plexiglas**	125.12	5.89	(37±4)	**STD.DEV**	**MTF %**	Yes
	Water	-0.07	5.44	1.6mm	41.60	5.80%	
	Difference	**125.19**		1.3mm	32.77	4.98%	
	Should be	120 ± 12		1.0mm	23.54	3.94%	
				0.8mm	13.22	2.28%	
120kV/260mA/5.000mm/1i/Small body/Rot Speed=0.1S/Axial							

Low contrast detectability						
	Mean CT #					
Object Size (mm)	**Mean**	**Std Err Mean**	**Std Dev**	**Err Std Dev**	**Specification**	**Contrast (HU) @95%CL**
3	-0.316	1.231	4.315	0.9	< 5.2HU	4.051
120kV/135mA/5.000mm/Speed=10.62/ Pitch=0.531:1/Rot Speed=0.1S/He+						

Licence/Unit no. 4231/28	Date Tested 31-08-2023	Tested By: A. Wessels	Technical Signatory - A Wessels	Technical & Quality Manager G Paton

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Worksheet #3

Test No. 145 Image Slice Thickness

SLICE THICKNESS			ALIGHMENT LIGHT ACCURACY		
Slice width	Specification	# of Visible Lines	Light/reference		Centered Y/N
10	10 ±1	n/a	IN'T Axial		Y
5	5 ±1	5.5	EXT Axial		Y
2.5	2.5 ±1	3	90/270 Laser		Y
1.25	1.0 ±0.5	1.5	0 Laser		Y

Worksheet #4

Modulation Transfer Function (MTF) Droege and Morin Method

Customer	Site	Date
DR A VAN DYK & PARTNERS	*BLOEMFONTEIN MEDI-CLINIC X-RAY DEPARTMENT - CT ROOM C/O PARFITT AVE & KELLNER STREET BLOEMFONTEIN*	*31 August 2023*
DoH Licence: 4231/28	*GE Healthcare System ID:*	*S/N: 88747WG1 S/N: 9543YC0*
GENERAL ELECTRIC LIGHTSPEED VCT	*ZA1000CT03*	*QC517*

	SD	Mean
BG (Water)	5.44	(0.07)
Max (Plexiglass)	5.89	125.12

M^o 125.19

N 8.02

1. Measure CT# and SD of background (bg) and max CT#
2. M_o = Mean of max minus bg
3. N = Mean noise
   $= \sqrt{(bg^2 + \text{max CT\#}^2)}SD$
4. Measure SD of each bar pattern
5. $MFT(f) = \frac{\sqrt{2}\pi}{4}\sqrt{\frac{SD(f)-N}{M_o}}$

MTF			
	5.80%	1.6mm	41.6
	4.98%	1.3mm	32.77
	3.94%	1.0mm	23.54
	2.28%	0.8mm	13.22

Licence/Unit no.	Date Tested	Tested By:	Technical Signatory - A Wessels	Technical & Quality Manager
4231/28	31-08-2023	A. Wessels		G Paton

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TEST No. 144 & 146 measurement worksheet for Beam Widths 0,5mm - 40mm

Date	[redacted]
31-Aug-23	
Room	
CT Room	[redacted]

Brand & Model	Serial Number	
GENERAL ELECTRIC LIGHTSPEED VCT	S/N: 88747WG1	S/N: 9543YC0
DoH Licence	Report No & System ID No	
4231/28	QC517	ZA1000CT03

Beam width (NxT): 5 mm
Pitch: 1

Performing Physicist
A.Wessels

Make sure Start Cell A1 is selected in Xi View before measuring values below.

Body Phantom		$CTDI_{100(centre)}$	$CTDI_{100(peripheral)}$ Average of 4 exposures	Exp 1	Exp 2	Exp 3	Exp 4	System Value		$CTDI_w$ Measured	$CTDI_{vol}$ Measured	Ref ± 15%
set kV	set mAs											
120	300	36.649 mGy	40.161 mGy	47.239	45.224	37.978	30.201	35.21	mGy	38.990 mGy	38.990 mGy	9.7%
100	300	14.349 mGy	30.021 mGy	32.055	32.328	23.721	31.979	22.51	mGy	24.797 mGy	24.797 mGy	9.2%
80	300	10.105 mGy	15.781 mGy	17.667	16.706	11.973	16.776	11.89	mGy	13.889 mGy	13.889 mGy	14.4%

Select Start Cell A50 in Xi View before measuring values below.

Head Phantom		$CTDI_{100(centre)}$	$CTDI_{100(peripheral)}$ Average of 4 exposures	Exp 1	Exp 2	Exp 3	Exp 4	System Value		$CTDI_w$ Measured	$CTDI_{vol}$ Measured	Ref ± 15%
set kV	set mAs											
120	300	83.335 mGy	90.943 mGy	98.457	93.525	77.354	94.436	75.35	mGy	88.407 mGy	88.407 mGy	14.8%
100	300	49.820 mGy	61.276 mGy	68.073	63.047	50.546	63.441	49.26	mGy	57.458 mGy	57.458 mGy	14.3%
80	300	27.400 mGy	34.361 mGy	37.784	35.512	27.702	36.445	27.41	mGy	32.041 mGy	32.041 mGy	14.5%

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GE Healthcare Technologies
INSPECTION BODY
DOH Licence no;1007

INSPECTION CERTIFICATE OF CONFORMANCE	
Bloemfontein [redacted] X-Ray Dept.	GE VCT
[redacted]	Date; 19-09-2013
User Site License No:4231/28	Unit S/No;88747WG1

THIS IS TO CERTIFY THAT THE DIAGNOSTIC X-RAY IMAGING DEVICE IDENTIFIED ABOVE CONFORMS TO THE TEST REQUIREMENTS AS DETAILED BELOW

The above device has been inspected and tested according to test requirements as documented in the GE Healthcare Technologies Inspection Body Test Procedure Register, CT-00-0001, and is found to function correctly, subject to the following remedial work to be undertaken by the parties designated in the action column.

ITEM NO:	REMEDIAL WORK DESCRIPTION	ACTION BY	DUE DATE	STATUS
				PASS

AUTHORISATION

Name:	Signature:	Date
Coloman Hendrik GE Healthcare Technologies IB:: Technical Signatory		19-09-2013

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Appendix G: DOH Acceptance test and routine test lists

	Bloemfontein [redacted]	GE VCT		
	Licence: 4231-/H	Ref: 2A100CC106	S/N 84/4/6W02	
	[redacted]	Code: DIAGNOSTIC QC (Modified January 2002) Version 7		
		Date: 10-03-2011		
1.1.2	Acceptance test and Routine test listed in this section must be performed by an Inspection Body approved by the Department of Health			
III.1.12.	Computed Tomography			Pass/Fail
46	Safety checks, red light/indicators	On acceptance & Daily	Must work properly	Pass
47	Image noise	On acceptance & Daily	Baseline + 10%	Pass
48	CT number values	On acceptance & Daily	Water baseline +- 5HU, Other materials baseline +-10%	Pass
49	Scan plane localisation from align light	On acceptance & 3 monthly	<=2mm	Pass
III.2.8	Computed Tomography			
140	Image Noise	On acceptance & 12 monthly	Baseline + 10% Inter-slice variation; Mean+ 10%	Pass
141	CT Number Values	On acceptance & 12 monthly	Water base+ 5 HU, Other materials baseline+ 10HU	Pass
142	CT Number uniformity	On acceptance & 12 monthly	Head Phantom: < + 10HU, Body Phantom: < + 20HU	Pass
143	High contrast spatial resolution	On acceptance & 12 monthly	Baseline + 20%	Pass
144	Computer tomography dose index (CTDI)	On acceptance & 12 monthly	Baseline + 10%	Pass
145	Image slice thickness	On acceptance & 12 monthly	Baseline + 20% or + 1mm, whichever is greater	Pass
146	CTDI vol for single slice or rotation	On acceptance & 12 monthly	< Reference dose.	Pass
	Ge Healthcare Technologies I.B.			
	Licence No :1007			
	Signatory: Coleman Henerik			
			Page 1/1	

Appendix H: Quality control tomography tests

Quality Control Test Tomography

GE Lightspeed VCT License 4231/28 S/N 88747WG1

BLFT[redacted] Date 19-09-2013

46. Indicators, radiation warning lights at entrance, mechanical and other safety checks.

					Pass/Fail
Radiation warning light at enterance working ?					Pass
Indicators working ?					Pass
Mechanical checks ?					Pass
Safety checks ?					Pass

47. Image Noise

N/A

	Spec				
	Mean CT #	STD. DEV	Mean CT#	STD. DEV	Uniformity diff
ROI CTR	0+/-3				
Edge Top	0+/-3				
Edge left	0+/-3				
Edge Right	0+/-3				
Edge Bottom	0+/-3				

48. CT number values

N/A

Low contrast detectability		
	Mean CT #	
	Top	Bottom
Membrane		
Water		
Difference		
Holes		
	Smallest hole	
	W/L = 30/Value for Water	

49. Scan plane localisation from alignment lights

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143. High Contrast Spatial resolution

Contrast Scale			Contrast Spatial		Slice Thickness	# Visible lines
	Mean CT #	STD.DEV				
Plexiglas	**119.29**	**4.58**	(37+/-4)	STD	10mm	**9.5**
Water	**-0.68**	**5.08**	1.6 mm	**38.66**	5mm	**5**
Difference	**119.97**		1.3 mm	**31.12**	1.25mm	**1.5**
Should be	120 +/- 12		1.0 mm	**23.54**	0.625mm	**1**
			0.8 mm	**12.32**		

144. Computed Tomography Dose Index(CTDI)

Computed Tomography Dose Index (CTDI)

Body

120KVp
260mA
1 sec

Head

120KVp
260mA
1 sec

n= 8 no of detectors
T= 1.25 slice thickness mm
L= 100 mm

Mearsurements :X

A =	**1.512** mGy		A =	**5.082** mGy	
B =	**3.006** mGy		B =	**5.93** mGy	
C =	**2.906** mGy		C =	**5.676** mGy	
D =	3 mGy		D =	**5.017** mGy	
E =	**2.967** mGy		E =	**5.961** mGy	
Avg Peripheral		**2.86975** mGy	**Avg Peripheral**		**5.621** mGy

Body

CTDI100= **1/nT x fX x L**
centre **15.12** mGy
CTDI100= **1/nT xfX x L**
Peripheral **28.6975** mGy

Head

CTDI100= **1/nT x fX x L**
centre **50.82** mGy
CTDI100= **1/nT xfX x L**
Peripheral **56.21** mGy

$$CTDIw(Body) = \frac{CTDI\ center + (2 \times CTDI\ peripheral)}{3}\ mGy$$

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QA VCT Bloemfontein[redacted];ZA1000CT03

Measurements done by Coloman Hendrik

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QA VCT Bloemfontein [redacted]:ZA1000CT03
Measurements done by Coloman Hendrik

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Appendix I: Letter from the biostatistician

Maryn Viljoen
Statistics Consulting Services

082 823 5731
maryn.viljoen1@gmail.com

Protocol & research methodology consultation | Ethical consultation | Database construction & capturing of data
Analysing data using statistical software packages (SAS Version 9.2) | Statistics consultation services to analyse and interpret data
Conveys results with statistical tables & figures where needed

The Chairperson: Health Sciences Research Ethics Committee (HSREC)
For Attention: Mrs. M.G.E. Marais
Block D, Room 104
Francois Retief Building
Faculty of Health Sciences
University of the Free State

26 July 2021

Title: "'A RETROSPECTIVE RESEARCH STUDY TO DETERMINE THE RELATION BETWEEN AN ELEVATED D-DIMER TEST AND A POSITIVE COMPUTED TOMOGRAPHY PULMONARY ANGIOGRAM TO CONFIRM PULMONARY EMBOLI."

Researcher: Kruger, R. A. (214037592)
Faculty of Health and Environmental Sciences
Department of Clinical Science: Programme Radiography
Central University of Technology, Free State
Bloemfontein

I have seen and read through this protocol. I gave input and recommendations and will be the biostatistician responsible for the analysis of the data.

Maryn Viljoen
M.Sc. Risk Analysis (UFS)
maryn.viljoen1@gmail.com
082 82 35 731

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Appendix J: Letter from the language editor

Declaration

26 July 2023

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Thesis: The Relation Between Elevated D-dimer Levels and a Positive Computed Tomography Pulmonary Angiogram to Confirm Pulmonary Emboli: A Retrospective Study

Student: Rochelle A. Kruger

I confirm that I edited the thesis, checked the references, and recommended changes to the text.

MA Language Practice

Hettie Human

WRITER | EDITOR | TRANSLATOR | INTERPRETER

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Appendix K: Turnitin report

The Relation Between Elevated D-dimer Levels and a Positive Computed Tomography Pulmonary Angiogram to Confirm Pulmonary Emboli

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