PANCREATIC TUMORS: A MULTICENTRE STUDY OF MULTIDETECTOR COMPUTED TOMOGRAPHY FINDINGS AND HISTOPATHOLOGIC CORRELATION IN NAIROBI, KENYA.

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DECLARATION

This research dissertation is my original work and has not been presented for a degree or an award in any other university.

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DEDICATION

To Jeremy, Jayden, Ricky and Meghan.

May you be inspired to be the best that you can be.

To my father, the late George Ogaro Omburo, for teaching me excellence.

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OPERATIONAL DEFINITIONS

Tumour size:	Largest tumour dimension in any of the orthogonal planes in centimetres.
Well circumscribed:	Having well defined margins.
Poorly circumscribed:	Having ill-defined margins.
Homogenous:	Having similar attenuation characteristics.
Heterogenous:	Having differing attenuation characteristics within the same lesion.
Smooth:	Lesion bearing a closed curvature with borders of the same circle.
Lobulated lesion:	Lesion bearing multiple curved edges that do not form borders of the same circle.
Irregular lesion:	Lesion that is of an uneven shape.
Capsule:	A sheath enclosing a lesion
Cystic:	Non-enhancing fluid filled structure with pre-contrast CT attenuation values of <20.
Solid:	Not of liquid or fluid consistency
Septations:	Strands within a cystic lesion.
Unilocular cyst:	Fluid filled lesion devoid of internal septations or a solid component.
Multilocular cyst:	Fluid filled lesion bearing internal septations.
Microcystic lesion:	Lesion whose largest cyst measures less than 2cm.
Macrocystic lesion:	Lesion whose largest cyst measures 2 cm or greater.
Attenuation:	Reduction in x-ray photon intensity as it courses through body tissue. It can be visually assessed as various shades of grey on a computed tomography image.
Hypoattenuating:	Bearing lower attenuation than normal pancreatic tissue on either pre-contrast or post contrast images on visual assessment.
Hyperattenuating:	Bearing higher attenuation than normal pancreatic tissue on either pre-contrast or post contrast images on visual assessment.

Isoattenuating:	Bearing similar attenuation with normal pancreatic tissue on either pre-contrast or post contrast images on visual assessment.
Rim enhancement:	Peripheral uptake of contrast by a lesion on contrast enhanced images.
Main pancreatic duct dilatation:	Maximal pancreatic duct diameter of greater than 3mm.
Common bile duct dilatation:	Maximal common bile duct diameter of greater than 7mm in patients aged less than 60 years and equal or greater than 9mm in patients aged more than 60 years.
Double duct sign:	Dilatation of both the pancreatic and common bile ducts.
Local invasion:	Infiltration of adjacent organs (duodenum, biliary tree, stomach, spleen, kidneys) by a pancreatic tumour.
Abutment:	Contact of 180 degrees or less between tumour and vascular circumference.
Encasement:	Contact of greater than 180 degrees between tumour and vascular circumference.
Calibre change:	Localised vascular narrowing, deformity of contour irregularity.
Thrombosis:	Non-enhancing filling defect within a vessel.
Regional nodal involvement:	Infiltration of lymph nodes located within the surgical field and that would be resected along with the primary tumour. The nodes may have a short axis diameter of greater than 1cm, may appear rounded, may have heterogenous attenuation or have central necrosis.
Metastasis:	Presence of spread to lymph nodes located outside the normal drainage route or that are not sited in the surgical field or presence of peritoneal nodules or ascites or presence of tumour in organs other than the adjacent organs, for example the liver, lung and bone.

ABBREVIATIONS AND ACRONYMS

BD-IPMN: Branch Duct- Intraductal Papillary Mucinous Neoplasm

CEA: Carcinoembryonic Antigen

CECT: Contrast Enhanced Computed Tomography

CM: Centimetres

CT: Computed Tomography

ERC: Ethics and Research Committee

ERCP: Endoscopic Retrograde Cholangiopancreatography

EUS: Endoscopic Ultrasound

FNAC: Fine Needle Aspirate Cytology

IPMN: Intraductal Papillary Mucinous Neoplasm

KGS: Kilograms

KNH: Kenyatta National Hospital

MCN: Mucinous Cystic Neoplasm

MDCT: Multi Detector Computed Tomography

MD-IPMN: Main Duct- Intraductal Papillary Mucinous Neoplasm

ML: Millilitre

MPD: Main Pancreatic Duct

MRI: Magnetic Resonance Imaging

NPV: Negative Predictive Value

NSCLC: Non-Small Cell Lung Carcinoma

PDA: Pancreatic Ductal Adenocarcinoma

PDAs: Pancreatic Ductal Adenocarcinomas

PNETs: Pancreatic Neuroendocrine tumours

PPV: Positive Predictive Value

RCC: Renal Cell Carcinoma

SCNs: Serous Cystic Neoplasms

SMA: Superior Mesenteric Artery

SMV: Superior Mesenteric Vein

SPN: Solid Papillary Neoplasm

SPNs: Solid Papillary Neoplasms

USA: United States of America

WHO: World Health Organisation

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ABSTRACT

Background: Pancreatic tumours have variable morbidities and mortalities dependent on the histological subtype, tumour grade and stage. These influence management strategies. Triple phase Multi-Detector Computed Tomography (MDCT) imaging has a role in tumour detection, staging, prognostication and treatment response assessment. There are limited studies on pancreatic tumour imaging characteristics and histologic types in Kenya and in Africa as a whole. Knowledge of MDCT imaging characteristics of different tumour types encountered in Kenya will impact on patient management strategies.

Objective: To analyse the MDCT imaging spectrum and histopathologic correlation of patients with pancreatic tumours at Kenyatta National Hospital, Plaza Imaging Solutions and German Medical Centre.

Methodology: This was a cross sectional study done at the radiology departments of KNH, Plaza Imaging Solutions and German Medical Centre in Nairobi, Kenya. Thirty-nine consenting patients found to have pancreatic tumours on triple phase pancreatic protocol MDCT imaging and who obtained histopathology results after tumour tissue sampling were recruited. A structured data collection tool was used to document the demographic data and MDCT pancreatic tumour imaging characteristics of the study participants. The most likely tumour type from evaluation of the MDCT imaging characteristics was documented as well as the histopathological diagnosis. Data analysis was done using the Statistical Package for Social Scientists software (version 25). The results were presented in tables, pie carts, and bar charts.

Results: A total of 39 participants were recruited into the study. The mean age of patients with pancreatic tumours was 58.4±13.9 years with 59% of them being female. Pancreatic ductal adenocarcinoma was the most prevalent tumour subtype at 87.2%. Pancreatic neuroendocrine tumour, solid pseudopapillary neoplasm and paraganglioma constituted 2.6% each while other pancreatic tumour subtypes were not represented. PDAs were mostly poorly circumscribed (91.2%), solid (85.3%), and located in the pancreatic head (55.9%). All the PDAs were hypovascular in the arterial and portovenous phases. Main pancreatic duct dilatation and distal pancreatic atrophy was seen in 61.8% and 58.8% of PDAs respectively. The double duct sign was only seen in 29.4%. Distant metastases were found in 47.1% of the tumours at presentation. The diagnostic accuracy of MDCT imaging for pancreatic ductal carcinoma was 94.9%. Sensitivity and specificity were 100% and 60% respectively, while the PPV and NPV were 94.4% and 100%.

Conclusion: This study has shown that pancreatic ductal adenocarcinoma is the most prevalent of the pancreatic tumour subtypes in Kenya. MDCT imaging using the pancreatic protocol had high accuracy consistent with studies conducted elsewhere and is therefore reliable in the diagnosis and exclusion of pancreatic ductal adenocarcinoma.

Recommendation: We recommend larger multicentre studies to evaluate the less commonly occurring pancreatic tumour subtypes. Retrospective studies focusing on the less common subtypes can be done to determine MDCT imaging features and diagnostic accuracy.

CHAPTER 1 INTRODUCTION

1.1 Background

The pancreas is a solid organ with endocrine and exocrine function that is located in the anterior pararenal compartment of the retroperitoneum. It has a head, neck, body, tail and uncinate process as its parts. The main pancreatic duct drains its secretions into the ampulla of Vater, which is a common channel with the common bile duct, then into the major papilla at the descending duodenum.

The pancreas can be imaged by various modalities including sonography, computed tomography and magnetic resonance imaging. Triple phase MDCT imaging is done to evaluate pancreatic neoplasms. Pre-contrast phase images are acquired prior to administration of intravenous non-ionic iodinated contrast. Pancreatic phase imaging is done 40 to 45 seconds after contrast administration while porto-venous phase images are obtained 60 to 70 seconds post contrast administration.

Due to its oblique orientation within the retroperitoneum, the pancreas is visualised on multiple axial planes on MDCT imaging. It has a feathery or lobulated outline, with homogenous soft tissue attenuation. It displays homogenous and maximal enhancement during the pancreatic parenchymal phase of post contrast imaging. The pancreatic duct may be visualised as hypodense linear structure traversing the parenchyma.

MDCT is the work horse for pancreatic imaging. It is relatively easily available, fast, non-invasive, has excellent spatial resolution, multiplanar capabilities and good diagnostic accuracy (1). It is able to evaluate the entire abdomen and provide information on locoregional and nodal involvement and presence of metastases. Its role includes; tumour detection and characterisation, staging, pre-operative prediction of tumour resectability, prognostication and assessment of tumour response post treatment(2,3,4). Definitive diagnosis of pancreatic tumour subtypes is achieved by histopathological evaluation. Tissue sampling for histological determination of pancreatic tumours is achieved by; percutaneous sonographic or CT guided biopsy, endoscopic retrograde cholangiopancreatography guided fine needle aspirate (ERCP FNA), endoscopic ultrasound guided FNA or intraoperative biopsy.

The 2010 World Health Organisation classification categorises pancreatic tumours into epithelial exocrine tumours, pancreatic neuroendocrine tumours, mature teratomas, mesenchymal tumours, lymphomas and secondary tumours. These are further subdivided into subtypes (Appendix 1). Pancreatic tumours have variable prognoses dependent on the histological type, grade, and stage. These influence management strategies. Pancreatic ductal carcinoma, for example, has a dismal prognosis. Resectable pancreatic adenocarcinomas require surgical resection while borderline resectable pancreatic ductal adenocarcinomas may require neoadjuvant chemoradiotherapy prior to surgery. Primary pancreatic lymphomas may be cured by chemotherapy. In contrast, microcystic neoplasms that are less than 4cm in size may be managed expectantly with serial follow up (5,6,7,8).

Some pancreatic tumours for example cystic pancreatic neoplasms, including IPMNs, MCNs, and SCNs are being increasingly diagnosed due to availability of cross sectional imaging and are often incidental findings in patients being imaged for other unrelated conditions(9). GLOBOCAN reported 458,918 new cases of pancreatic cancer worldwide and 432,242 mortalities for the year 2018. The Kenyan estimates for the same year were 735 new cases and 719 deaths. The 5-year prevalence was 536(10). Pancreatic cancer incidence was highest in Europe at 7.7 per 100,000 people and North America at 7.6 per 100,000 people while the lowest incidence was reported to be in Africa with an incidence of 2.2 per 100,000 people (11).

Limited scientific studies exist on pancreatic tumour subtypes and MDCT imaging features in Kenya and indeed in the African continent. This study aims at increasing knowledge among radiologists and hepatobiliary surgeons on the different tumour subtypes that occur in the Kenyan population, their MDCT imaging spectrum and diagnostic accuracy.

CHAPTER 2 LITERATURE REVIEW

2.1 Multidetector Computed Tomography

Multidetector computed tomography scanners are composed of a gantry, an x-ray tube and multiple rows of detectors. These multiple rows of detectors when exposed to the x-ray beam provide separate channels of data that can be used to construct axial images. Over time, different generations of scanners have become available, from the 2, 4, 8, 16, 32, 64, 128, 256, 320 and the 640 detector scanners due to technological advancement. The higher slice CT machines are able to cover a larger anatomic area with a single rotation and have a faster scan time.

Goshima et al 2011, compared different generations of MDCT machines in pancreatic evaluation. They reported that 64 and 320 slice scanners had comparable depiction of the celiac, splenic, SMA and peripancreatic small arteries, and of the pancreatic parenchyma, main pancreatic duct and focal pancreatic lesions. Both scanners had acceptable image quality(12). Ewaidat et al 2018, found that the image quality obtained by 16, 32 and 64 slice scanners in the evaluation of the abdomen was acceptable and sufficient for adequate interpretation(13).

2.2 Pancreatic Ductal Adenocarcinoma

Pancreatic ductal carcinoma is the commonest and most lethal of the pancreatic tumours. It is an aggressive tumour with poor prognosis. Accurate, timely diagnosis and determination of tumour resectability cannot be over-emphasized. The highest incidence is in Western Europe and North America while the lowest rates are in Africa and Asia, with age-standardised incidence rates estimated to between 2.8/100,000 and 7.2/100,000 population(14).

Several studies have shown that PDA occurs more commonly in males. Patients are usually in their seventh decade of life. A retrospective study done by Costache et al, 2016 in Romania on 100 patients with histologically confirmed pancreatic ductal carcinoma showed a male predilection of 61% and a mean patient age of 64 years(15). A larger study conducted in Korea of 644 patients done by Kim et al, 2010 reported a comparable male predilection of 60.9%. The mean patient age was 60 years(16). Another study done in North Africa by Sellam et al in 2015 found the median

age of 160 patients with carcinoma of the pancreas to be 62.2 years with a male preponderance of 65.6%(17).

Typically, PDAs are hypoattenuating hypoenhancing solid tumours on MDCT imaging. Some tumours are isoattenuating and may be suggested by the presence of secondary signs. Most PDAs are sited in the pancreatic head but can also arise in the other parts. A systematic meta-analysis by Shirkhande et al 2012, that included 66 articles found that pancreatic carcinomas were mainly hypoattenuating on the arterial phase with only 11% of the tumours being isoattenuating. These isoattenuating tumours were suggested by secondary signs like pancreatic duct and common bile duct dilatation(1). According to Kim et al, isoattenuating tumours comprised 5.4% of 644 pancreatic adenocarcinomas. The commonest secondary sign was pancreatic duct cut off with proximal pancreatic duct dilatation (86.7%), followed by distal CBD luminal narrowing with proximal dilatation (80%). Others were pancreatic duct cut off with atrophy of the distal pancreatic parenchyma, focal pancreatic contour bulge, presence of retention cysts within the pancreas and a focal area of fat sparing in a pancreas with fatty change (16). Yoon et al reported that isoattenuating tumours were commonest in smaller tumours of less than 20mm diameter than in larger tumours of 20-30mm (P= 0.033) and in well differentiated tumours than moderately and poorly pathologically differentiated tumours (P=0.001). Most of the isoattenuating tumours (88%) showed secondary signs. The commonest sign was pancreatic or CBD dilatation (63%). Most of the tumours were located in the pancreatic head (70% of the surgically confirmed tumours and 64% of the pathologically determined tumours)(18).

Multidetector computed tomography imaging has been found to have good diagnostic accuracy for PDAs in several studies. Shirkhande et al reported MDCT sensitivity and specificity of 75 to 100% and 70 to 100% respectively in the diagnosis of pancreatic carcinomas(1). The sensitivity was higher for tumours exceeding 2cm (98%) than for those less than 2cm (68-77%)(1). Costache et al determined that MDCT had a diagnostic accuracy of 83.3%, sensitivity of 81.4% and specificity of 43%, with higher accuracy for tumours greater than 20mm in size.

2.3 Intraductal Papillary Mucinous Neoplasm

This is a mucin producing cystic neoplasm of the pancreas that is of epithelial origin. Two types are recognised according to localisation within the pancreatic duct system; Main Duct- IPMN and

Branch Duct- IPMN. All IPMNs have potential for malignancy and as such, surgical resection is usually recommended(19).

The incidence and prevalence rates of intraductal papillary mucinous neoplasm have been described in different regions, among different cohorts of patients. In France, 6.6% (14/315) of patients awaiting liver transplantation had incidental IPMNs, which underpinned the need for early screening of patients with chronic liver disease(20). However, in a review of data from the Rochester Epidemiology Project, Reid-Lombardo reported significantly lower results, with the incidence and point prevalence of intraductal papillary mucinous neoplasm estimated to be 2.04/100,000 cases and 25.96/100,000 persons, peaking among elderly (60+ years) persons [99.10/100,000] (21).

Intraductal papillary mucinous neoplasms are more commonly diagnosed in elderly patients. A retrospective study done by Kang et al in Korea that included 129 patients with pathologically confirmed IPMN found a mean age of 64.5 years, with a 59.7% male preponderance(4). Valsangkar et al reported a mean age of 69 years for patients with IPMN in the USA, with BD-IPMN having a female preponderance and MD-IPMN affecting male and female patients equally(9).

Computed tomography imaging features of IPMNs include unilocular or multilocular cystic lesions bearing lobulated margins that communicate with the pancreatic duct system, dilatation of the MPD and bulging of the duodenal papilla(15,23). Presence of a mural nodule within a pancreatic duct has also been reported(24). The pancreatic head and uncinate process are common locations for the tumour. Kang et al found that most of the tumours were located in the uncinate process (38%) followed by the body, head, tail and neck in descending order of frequency(4). According to Valsangkar et al, the mean tumour diameter was 2.88cm for MD-IPMN and 2.91cm for BD-IPMN. The pancreatic head, uncinate process and neck were the preferred sites of involvement(9).

Song et al, 2007 found an MDCT sensitivity of 80.6%, specificity of 86.4%, PPV of 89.3% and NPV of 76.1% in differentiating IPMN from other cystic pancreatic tumours(23).

2.4 Mucinous Cystic Neoplasms

These are also mucin producing cystic neoplasms of the pancreas that are of epithelial origin. They can be benign (mucinous cystadenoma) or malignant (mucinous cystadenocarcinoma). Mucinous cystic neoplasms constitute 1% of pancreatic tumours and about 10-15% of all pancreatic cystic neoplasms (25). It is less rare than SCNs and IPMNs, but has a high risk of malignancy [6%-46%] (26).

These tumours commonly occur in females in their fifth decade of life. Crippa et al, 2008, in a multicentre study done in the USA and in Italy that included 163 patients, reported a median age of 45 years and a 97% female preponderance(27). According to Valsangkar et al who did a retrospective study of 851 patients with cystic pancreatic neoplasms in the USA there was an 84% female preponderance and a mean age of 51 years among patients with MCN(9). Another retrospective study of 60 patients with pathologically proven MCN in France done by Baleur et al showed a 98.3% female predilection. The median age of patients with benign MCN was 42 years, and that of malignant MCN was 48 years(28).

Mucinous cystic neoplasms can be unilocular or multilocular macrocystic lesions(29). The cysts do not communicate with the pancreatic duct unlike in IPMN. They have a predilection for the pancreatic body and tail(9)(27)(28)(29). Valsangkar et al reported a mean tumour diameter of 4.41cm (9). Comparable findings were shown by Crippa et al on pathological evaluation with the median diameter being 5cm(30). All the patients in Crippa et al's study had solitary lesions and 17.5% of them were found to have malignant lesions. The findings associated with malignancy were tumour dimension of greater than 60mm and presence of nodules(27).

Baleur et al reported a maximal tumour diameter of 3.5cm for benign MCN and 80mm for malignant MCN; the difference in tumour size being statistically significant ($P<0.001$). Other CT imaging characteristics included, presence of a mural nodule (18.3%), septa (55%),wall calcification (23.3%) and peripancreatic adenopathy (1.7%)(28). Spence et al also reported presence of mural nodules, septations, a capsule and calcifications(29).

In a meta-analysis of 12 studies that included 332 participants, analysis of CEA at 5 ng/mL cut off returned a sensitivity of 50%, specificity of 95%, positive and negative predictive values of 94%

and 55% respectively, while CA 19-9 levels in 136 individuals had a high specificity (98%) but poor sensitivity (19%), a PPV of 94% and NPV of 38% using a cut off of <37U/mL(31). Radiological diagnostic accuracy findings are limited in literature.

2.5 Serous Cystic Neoplasms

These benign pancreatic tumours (serous cystadenomas) may rarely transform to malignant tumours (serous cystadenocarcinomas). A prevalence of 0.1% of malignant SCNs has been reported in literature(32). It is important to distinguish SCNs from other pancreatic cystic neoplasms like MCN and IPMN which have higher rates of malignant transformation and are hence best treated by surgical resection(5). Reported prevalence in the literature is from histopathologic analysis is about 3.7% of pancreatic cystic neoplasms(33).

Serous cystic neoplasms are more commonly found in middle aged and elderly women. A large multinational study done by Jais et al, 2015 including 2,622 patients with pathologically or radiologically diagnosed SCNs, reported 74% female predilection and a median age of 58years (range 16 to 99years)(32). Galanis et al, 2007 reported a comparable female predilection (75%) and a mean age of 62.1years (26 to 89years) with a study population of 158 patients (34).

They are commonly microcystic tumours located in the pancreatic head and may contain calcifications. Sun et al, 2009 found only 38.9% of SCNs had the typical microcystic pattern with the remaining being hypervascular solid with or without a cystic component, unilocular, oligolocular cystic, finger like cystic or pleomorphic(35). In the study conducted by Galanis et al, 0.6% had lymph node involvement, and these patients had benign disease. The mean tumour size was 5.1cm. The pancreatic head was involved in 42% of the patients, body or tail in 48%, proximal neck or body in 7% and diffuse pancreatic involvement was found in 3%(34). Jais et al reported 0.1% cases of serous cystadenocarcima with the liver and hepatic artery lymph nodes as metastatic sites. Most of the tumours were radiologically microcystic (55%) with the rest being macrocystic, mixed macro and microcystic or solid. Microcystic tumours were defined as having cysts of less than 2cm, while macrocystic were 2cm or larger in size.

Calcifications were identified in 15% of the tumours. Majority of the tumours were located in the head and uncinate process (40%). There was associated dilatation of the main pancreatic duct in

11% of the tumours(32). Zhong et al, 2019 reported specific EUS imaging characteristics of SCNs to be a location in the pancreatic head, lobulation, thin wall and presence of more than two septations in pancreatic cystic tumours.

The diagnostic scheme for serous cystic neoplasms has been reported in literature as robust and accurate. Using preoperative computer-aided MDCT based diagnosis, Wei et al, 2019 reported the sensitivity and specificity of SCN detection to be 68.6% and 70.9% respectively. The findings were comparable to those of independent validation with sensitivity of 66.7% and specificity of 81.8%(36). Zhong et al, while studying the differential diagnosis of pancreatic cystic neoplasms reported slightly higher results with endoscopic ultrasound [sensitivity and specificity of 84.2% and 80.6%], with the PPV and NPV for diagnosis found to be 84.2% and 80.6% respectively for the diagnosis of SCNs(37).

2.6 Pancreatic Neuroendocrine Tumours

These are rare pancreatic neoplasms that tend to be indolent and have potential for malignant transformation. They can either be functioning, meaning that they secrete hormones that may cause symptomatology, or may be non-functioning.

Various literature report variable sex preponderance with patients being commonly in the sixth decade of life. A study done by Halfdanarson et al, 2008 in the USA reported an annual incidence of 2.2 per 1,000,000, being higher among males [2.6/1,000,000] than females [1.8/1,000,000]. Its incidence rate is thought to be underreported because of its low detection rate (38). A study conducted in Japan done by Hijioka et al, 2014 reported a median age of 59 years with 54.5% of the patients being male and 45.5% being female(39). Other studies have reported a slight female predilection. Gallotti et al, 2013, in a retrospective study in the USA reported mean patient age of 56.7 years with a female preponderance of 51.6% (40). Kawamoto et al, 2013 found a mean age of 55.5 years and a slight female predilection of 51.35%(41).

Pancreatic neuroendocrine tumours are commonly solid but may be cystic or have both cystic and solid components. They tend to be hypervascular compared to the normal pancreatic parenchyma on post contrast images but can also be hypovascular. Gusmini et al, 2007, reported that most pancreatic neuroendocrine lesions confirmed on immunohistochemistry were hypervascular on

post contrast MDCT imaging (45.6%) with the remainder being heterogenous or hypovascular. Twenty two percent of the patients had hypervascular liver metastases. There were no hypovascular liver metastases reported(42). The imaging characteristics reported by Gallotti et al included a mean tumour diameter of 3.32cm and the tumours were majorly entirely solid (63%). In the tumours with cystic changes (37%), some had uniform or irregular walls and some had solid components. The commonest location was the tail (47%). Vascular and lymph node involvement, MPD dilatation and presence of calcification were highly suggestive of malignant PNETs. Ten percent of the patients had metastases to the liver. On pathological assessment 53% of the tumours were found to be non-benign (40).

Kawamoto et al reported a mean tumour size of 3.0cm (range of 0.7 to 13.1cm). Most tumours were completely solid (69.9%) with 14.1% being completely cystic and the rest were mixed solid and cystic. Internal nodular components within the cystic areas and septations were uncommon findings. Rim enhancement exceeding the normal pancreatic parenchymal enhancement was seen in 85% of predominantly cystic tumours(41). Hijioka et al found that 11.6% of PNETs were pathologically determined to be malignant according to WHO classification. Of the 11 pancreatic neuroendocrine carcinomas, 82% were hypovascular on post contrast MDCT imaging. Most (72%) of the patients with malignant disease had liver metastases at initial diagnosis and 88% of these were similarly hypovascular. Majority of the tumours were located in the pancreatic body (45.6%). The MPD was dilated in 57% of patients with tumours located in the head and body. The median tumour size was 3.5cm(39). This study was limited by a small sample size of 11 pathologically determined pancreatic neuroendocrine carcinomas. In a study that compared hypovascular PNETs and pancreatic ductal adenocarcinomas, which tend to be hypovascular as well, Ren et al reported that the hypovascular PNETs had higher frequency of a well circumscribed margin and a lower frequency of MPD dilatation and local invasion ($p<0.05$). This could be due to the scirrhous nature of PDAs. Hypovascular PNETs also had higher attenuation and higher tumour to pancreas enhancement ratio compared to PDAs(43).

Contrast-enhanced CT scans have demonstrated a high sensitivity and specificity in diagnosis of pancreatic neuroendocrine tumours. While evaluating gasteroenteropancreatic tumours using nuclear medicine and radiological imaging in 2012, Sundin Anders found imaging accurate for diagnosing tumours that are >2cm wide with a sensitivity and specificity range of 63%-82% and

83%-100% reported. However, the sensitivity drops markedly when tumour sizes were less than 2cm(44). Ren et al reported slightly lower results for specificity in 2019 [sensitivity of 83.3–88.9% and specificity of 61.6%–77.0%] in a Chinese study that used contrast enhanced MDCT to distinguish hypovascular PNETs from pancreatic ductal adenocarcinomas(43).

2.7 Solid Pseudopapillary Neoplasm

Solid pseudopapillary neoplasms are low grade pancreatic tumours with good prognosis that have a predilection for young women. It is an uncommon entity that accounts for 0.9-2.7% of exocrine neoplasms and 2%-3% of pancreatic neoplasms(45). Several studies have shown that SPNs typically occur in female patients in their third and fourth decades. Paediatric and elderly patients are also afflicted. In a retrospective study by Raman et al of 51 patients with histologically proven SPNs, 84% were female, and had a mean age of 33years(46). Yu P-F et al reported a female predilection of 89.3% with lower mean age of 27.2 years in a meta-analysis of Chinese literature with a larger sample population of 553 patients with pathologically confirmed SPNs(47). A meta-analysis of English literature detailing 718 SPNs and spanning over 70 years reported higher female predilection of 90.72%, with a mean age of 21.97 years (range 2 to 85years)(48). A retrospective study done in Singapore by Anil et al reported all patients with histologically confirmed SPNs to be female with a mean age of 32 years.

Various investigators have described the imaging characteristics of SPNs. Raman et al reported that most SPNs were large (mean size of 5.34cm), well-defined, heterogenous tumours with an enhancing capsule. They ranged from entirely cystic to entirely solid, with some being mixed cystic and solid, and showed even distribution between head, body and tail (30%, 30%,40%). Peripheral and central calcifications occurred often (46.7%). There was no associated biliary nor pancreatic duct dilatation(46). The mean diameter of tumours in the Chinese study by Yu P-F et al was 7.87cm, most tumours were heterogenous (60.12%), while 15.63% were cystic and 24.25% were solid. Most SPNs were located in the head (39.8%) with some extra pancreatic sites seen (retroperitoneum, mesentery and left adrenal gland). 9.2% of patients were diagnosed to have malignant SPN with metastasis and invasion with the structures involved including the liver, spleen, diaphragm, omentum, peritoneum, stomach, duodenum, colon, left kidney, portal vein, splenic vein and SMV(47). According to Papavramidis et al, most SPNs were located in the tail

(35.9%). The mean diameter was 6.08cm (range of 0.5cm to 34.5cm) and sites of metastasis were similar to that reported by Yu PF et al with the addition of the lung.

A study by Anil et al found that most lesions were in the tail and were larger in size compared to those occurring in the head (12.6cm versus 4.0cm). This was thought to be due to absence of obstructive symptoms that are usually associated with pancreatic head tumours. 80% of the tumours were mixed cystic and solid, 50% were encapsulated, 40.5% displayed calcification and all the tumours were hypo enhancing on post contrast images. 70% of the tumours were heterogeneously hypo-enhancing. The smaller tumours (measuring about 3cm in size) were purely solid and homogenously hypo-enhancing. 30% of the tumours showed invasion of the spleen(49). The limitation of the study by Anil et al was a small sample size of 10 patients.

In published literature, the sensitivity and specificity of pre-operative endoscopic ultrasound as a diagnostic tool for solid pseudopapillary neoplasms has been estimated to reach 90% and 94% respectively (50). The diagnostic performance of CT imaging demonstrated 100% sensitivity, but was not as specific as the EUS technique (63.5%) (51).

2.8 Secondary Tumours

Though the occurrence of secondary tumours in the pancreas is rare, accurate diagnosis is imperative as it impacts on the management strategy. The frequency of secondary pancreatic tumours is reported to vary from 2 to 5% (52,53). Several studies have found secondary tumours to be common in elderly patients in their sixth to seventh decades of life. Tsitouridis et al, 2009, in a prospective study of 11 patients from Greece found that the majority were female (63.6%), and the mean age of the patients was 62.45 years(54). A retrospective study done in China by Shi et al, 2015, that incorporated 18 patients, however reported a male predominance of 66.7%(55) and a mean age of 57.1 years. A retrospective study done by Crippa et al, 2006 with histologically confirmed pancreatic metastases reported that out of 13 patients, 69.2% were female, while 30.8% were male. The median age was 59 years(30).

Computed tomography imaging appearances are varied including solitary, multifocal or diffuse lesions that may be hypovascular or hypervascular and showing homogenous, heterogenous or peripheral enhancement. Renal cell carcinomas and lung cancers are the most common primary

sites. Tsitouridis et al's study reported lung cancer as the most common primary (63.3%), followed by breast cancer (27.3%) and RCC (9%)(54). Only 45.5% of the patients in this study obtained histological confirmation however. The diagnosis for the others was based on clinical history, follow up and imaging findings. The mean tumour size was 2.75cm. Most tumours had solitary lesions (63.6%) that were well defined (81.8%). Diffuse involvement was seen in 1 patient (0.09%), who had breast carcinoma. 90.9% of the tumours were solid, with only 1 (whose origin was a small cell lung carcinoma) being cystic. Rim enhancement was shown in 72.7% of the tumours. 27.3% showed homogenous enhancement and these were from lung carcinoma and RCC. Most of the tumours were located in the body (33.3%), followed by the head and tail (each 27.8%) and the neck (11.1%)(54). According to Shi et al, 2015 lung carcinoma was the most common primary site (38.8%), with others being gastrointestinal carcinoma, RCC, osteosarcoma, cardiac sarcoma, and neuroendocrine ethmoid sinus carcinoma in order of decreasing frequency. All the tumours were confirmed on histology. Tumour size ranged from 1.1 to 8.1cm with 66.7% being solitary lesions. 91.7% of the tumours were well circumscribed.

Majority of the tumours were solid (97.2%) with approximately half (51.4%) being hypodense on pre-contrast MDCT imaging. Only one tumour that was from an osteosarcoma primary was cystic, with an enhancing capsule and calcification observed within the tumour. NSCLC and gastrointestinal tumours were found to be small sized, well defined and displayed homogenous or rim enhancement. Cardiac sarcomas and renal cell carcinomas were found to be hypervascular with RCC secondaries being multiple and showing homogenous or heterogenous enhancement.

Majority of the metastases were located in the pancreatic tail (47.2%)(55). Renal cell carcinoma was found to be the commonest primary (38.5%) by Crippa et al, followed by breast (23.1%) and by endometrioid carcinoma of the ovary, colonic adenocarcinoma, jejunal adenocarcinoma, melanoma and NSCLC (each 0.08%). Majority of the tumours were hypo-vascular (61.5%) while 38.5% were hypervascular (including 1 breast lobular carcinoma and 4 RCC metastases). Most patients had solitary lesions (92.3%), while only one (with NSCLC) had multiple lesions. The most common tumour location was the pancreatic head (61.5%) unlike the studies by Shi et al (pancreatic tail) and Tsitouridis et al (pancreatic body)(30).

2.9 Pancreatic Lymphoma

Primary pancreatic lymphomas are uncommon malignant tumours of the pancreas that are of hematopoietic origin. They constitute 0.2-2% and 5% of extra-nodal lymphoma and pancreatic masses respectively(56) and have been found to be more prevalent in males than females(57).

A retrospective study done by Sadot et al, 2015 of 44 pathologically confirmed pancreatic lymphomas showed a slight male predilection of 55% and a median age of 62.5 years (range of 15 to 85years (8). Comparable male predominance of 58.3%, and median age of 65.5 years was reported in a retrospective study done by Ramesh et al, 2014 in the United States of America, though with a smaller sample size of 12 (58).

Primary pancreatic lymphomas are homogenous, poorly enhancing, focal or diffusely infiltrating solid tumours that demonstrate extrapancreatic infiltration, with or without nodal involvement(7). They rarely demonstrate heterogeneity and vascular involvement and have a predilection for the pancreatic head. Some reports indicate the body and tail to be commonly involved(59). Minimal pancreatic duct dilatation may occur(59).

According to Sadot et al, the median tumour size was 7.9cm. Majority of the tumours were focal (90%) and were well circumscribed. The head and uncinate process were the most common location (54%). There was associated peripancreatic lymphadenopathy (65%), with majority of tumours being unresectable (66%) at diagnosis(8).

2.10 Pancreatoblastoma

Pancreatoblastoma is a rare malignant tumour of epithelial origin. It accounts for 0.2% of all pancreatic tumours(60). It is the commonest pancreatic neoplasm in the paediatric age group. This tumour comprised 17.2% of paediatric pancreatic malignancies in the USA, with only 10 documented cases spanning over 31 years (61). Ozcan et al, 2014 reported only 2 cases over a time period of 22 years, comprising 13.3% of paediatric pancreatic malignancies(62).

Pancreatoblastoma is prevalent in the first decade of life (60). The mean age at diagnosis is about 5 years [range 1 to 8 years] (63). Occurrence in adults is very rare. Case series and reports are

documented in literature (64,65) with only 35 cases reported so far(66). Several studies have reported a male predilection ranging between 51% to 66.7% (66,67,68,69).

Suggestive CT imaging appearances that have been documented include well defined heterogenous, multilocular masses with areas of haemorrhage, necrosis and calcification that demonstrate heterogenous enhancement on post contrast imaging (65,70,71). They may be solid, cystic or mixed cystic and solid (65,72). The tumours are often large and may range from 3 to 15cm (70,72). Encasement of adjacent blood vessels, nodal involvement, ascites and metastatic lesions, especially to the liver, omentum and peritoneum occur (70,71,73).

Several investigators have reported the pancreatic head as the most common location (66,72,73). Roebuck et al, 2001 found pancreatoblastoma involved the pancreatic body and tail or the entire pancreas(70). Associated biliary / and or pancreatic duct dilatation was reported by Roebuck et al, Ozcan et al and Montemarano et al.

2.11 Conceptual Framework

The aim of the study was to demonstrate the prevalence of subtypes of pancreatic tumours in a sample of Kenyan patients with pancreatic neoplasms and establish tumour imaging characteristics and the diagnostic accuracy of MDCT imaging for these tumours. The diagnostic accuracy of MDCT may be influenced by tumour characteristics. Demographic characteristics of patients such as age and gender have been found to have an association with certain pancreatic tumour subtypes. Mucinous cystic neoplasms, serous cystic neoplasms and solid pseudopapillary neoplasms have a female predilection. Pancreatic ductal adenocarcinomas, intraductal papillary mucinous neoplasms, and serous cystic neoplasms are predominantly tumours of the elderly (6-7th decade of life), while pancreatoblastomas are predominantly paediatric tumours.

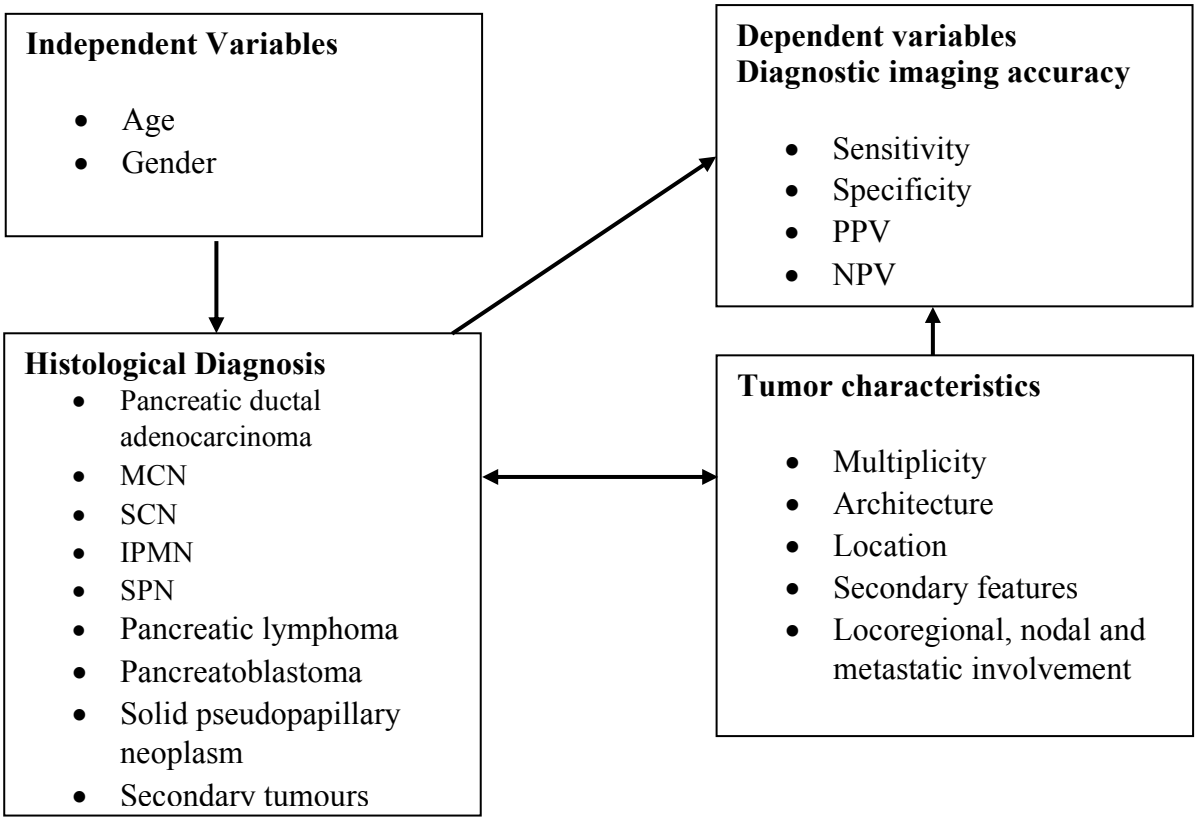


Figure 2.1. Conceptual framework

2.12 Study Justification

There are limited studies on pancreatic tumour prevalence and imaging characteristics in Kenya. This study aims to add on to the knowledge of MDCT imaging characteristics of different tumour types encountered in Kenya. Different pancreatic tumour types present different risks to the patient in terms of malignant transformation, morbidity and mortality. The various methods of sample collection for histopathological diagnosis have the disadvantage of being invasive. It is therefore imperative that timely and accurate radiological diagnostic evaluation is undertaken. The study findings will increase awareness among reporting radiologists on the imaging characteristics of different pancreatic tumour types in Kenyan patients.

2.13 Study Question

What are the MDCT imaging findings and diagnostic accuracy in the evaluation of pancreatic tumours in the study population?

2.14 Study Objectives

2.14.1 Broad Objective

To analyse the demographic characteristics, MDCT imaging spectrum and diagnostic accuracy in various pancreatic tumour subtypes in the study population.

2.14.2 Specific Objectives

1. To determine the prevalence of different pancreatic tumour subtypes in the study population
2. To determine the demographic profile of pancreatic tumours in the study population.
3. To evaluate the MDCT imaging characteristics of the different pancreatic tumours in the study population.
4. To establish the diagnostic accuracy of MDCT imaging for pancreatic tumours in the study population with histopathological diagnosis as the reference standard.

CHAPTER 3 METHODOLOGY

3.1 Study Design

A prospective cross-sectional study that was carried out at KNH, Plaza Imaging Solutions and German Medical Centre.

3.2 Study Setting

KNH is a National Teaching and Referral hospital located in Nairobi, Kenya. It is the teaching hospital of University of Nairobi, College of Health Sciences. It is one of the two tertiary referral facilities in the entire country and as such it serves the majority of the Kenyan population requiring specialised health care. Plaza Imaging Solutions and German Medical Centre are privately owned imaging centres located within Nairobi, Kenya. Some of the patients under the medical care of private practitioners have imaging done at these privately-owned imaging centres prior to referral to KNH for definitive management.

3.3 Study Population

Patients found to have pancreatic tumours on MDCT imaging done at Kenyatta National Hospital, Plaza Imaging Solutions and German Medical Centre.

3.4 Inclusion Criteria

- All consenting patients confirmed to have pancreatic tumours on MDCT imaging done for clinical suspicion of pancreatic tumours.
- All consenting patients known to have pancreatic tumours diagnosed on other imaging modalities and presenting for MDCT for further tumour characterisation.
- All consenting patients found to have incidental pancreatic tumours on MDCT imaging done for unrelated conditions.
- All paediatric patients found to have pancreatic tumours on MDCT imaging with assent / guardian consent given.

3.5 Exclusion Criteria

- Patients with known histopathological diagnosis prior to imaging.
- Patients with discrepant histopathological diagnosis and whose tissue slides or blocks were not available for reevaluation.

3.6 Sample Size Determination

According to Ballarin et al (2011), secondary pancreatic tumors constitute 2-5% of all malignant pancreatic tumors(53). The upper limit (5%) was used to calculate a sample size (n) at 95% CI and precision of 5% using the formula by Fisher (1981). Currently at the three imaging centres, approximately 10 patients are diagnosed to have pancreatic tumours based on MDCT imaging on a monthly basis. This amounts to approximately 80 patients within the study period of 8 months.

Formula:

$$n = \frac{Nz^2pq}{E^2(N-1) + z^2pq}$$

n: Sample size

p: Prevalence of secondary pancreatic tumours

z: Normal variate for alpha

q: 1-p

E: Precision

N: Population size

Assumptions:

E = 5%

P = 5% (Ballarin et al (2011))

N = 80

Z^2 = 1.96

Estimated sample size:

$$n = \frac{80\ x\ 1.96^2\ x\ 0.05\ x\ 0.95}{0.05^2(80-1) + (1.96^2\ x\ 0.05\ x\ 0.95)} = 39$$

Required sample size (n) = 39

3.7 Patient Recruitment

The principal investigator recruited thirty-nine participants among patients found to have pancreatic tumours on MDCT imaging and who eventually obtained a histopathological diagnosis. Study objectives were explained to the potential participants. Written consent was obtained from those that were willing prior to recruitment.

3.8 Sampling Procedure

Convenience sampling method was used.

3.9 Consent Procedure

Pre-designed consent forms with information on the study purpose, procedure, potential benefits and possible risks were used to obtain written informed consent. Any questions or concerns regarding the study that were raised were addressed. The process was voluntary and free from coercion. Patients who opted out received routine care without discrimination.

3.10 MDCT Protocol

KNH radiology unit has a 128 slice Siemens CT scanner and a 64 slice Neusoft CT scanner. Plaza Imaging Solutions and German Medical Centre each have a 16 slice Siemens CT scanner. All the machines in the three centres have multi-row detectors. All the centres used the triple phase pancreatic protocol (pre-contrast, pancreatic and porto-venous phases) to image patients with suspected pancreatic tumours. The patients were fasted for at least six hours prior to the examination being done. One litre of negative contrast (water) was given orally over a duration of one hour prior to imaging to distend the gastric wall. The patients were positioned supine at the center of the gantry with the feet first. A scanogram was first acquired to aid in planning the anatomical range and to determine the x-ray tube current. Determination of initiation of scanning for the different phases was done by the automatic bolus tracking method. A region of interest was placed within the descending aorta at the level of the diaphragmatic dome. The CT scanner was then set to automatically start acquiring post contrast images at a predetermined time after an attenuation of 100 Hounsefield Units of aortic enhancement was attained. Non-ionic iodinated contrast media was administered by a power injector through an 18-gauge intravenous cannula

placed at either antecubital fossa at a dosage of 80 to 100mls and a rate of 3 to 4ml/sec. Normal saline (20mls) was used to flush the venous access immediately after contrast administration. On average, pancreatic phase imaging was done at 40 to 45 seconds and porto-venous phase imaging at 60 to 70 seconds after contrast administration. Axial images acquired were reconstructed using a slice thickness of 1mm to obtain sagittal and coronal images. The table below summarises the technical parameters.

Table 3.1. MDCT pancreatic protocol parameters

TECHNICAL PARAMETERS	NEUSOFT 128 SLICE CT SCAN MACHINE (KNH)	SIEMENS 16 SLICE CT SCAN MACHINE (PLAZA IMAGING SOLUTIONS)	SIEMENS 16 SLICE CT SCAN MACHINE (GERMAN MEDICAL CENTRE)
Kilovoltage	120	120	110-130
Effective milliamperes	180	200	160-180
Phases	Precontrast Arterial Porto-venous	Precontrast Arterial Porto-venous	Precontrast Arterial Porto-venous Delayed
Slice Thickness (mm)	5mm	5mm	5mm
Reconstruction thickness (mm)	1mm	1mm	1mm
Increment (mm)	Arterial: 1mm Porto-venous: 5mm	Precontrast: 0.5-0.75mm Arterial: 0.5-0.75mm Porto-venous: 0.5-0.75mm	Precontrast: 0.5-0.75mm Arterial: 0.5mm Porto-venous: 0.5-0.75mm Delayed: 0.5-0.75mm
Image Order	Cranio-Caudal	Cranio-Caudal	Cranio-Caudal
Oral Contrast	1 litre of water over one hour	1 litre of water over one hour	1 litre of water over one and a half hours
Intravenous Contrast Type and Volume (ml)	80-100ml of Iohexal 350 or Iopromide 300	80-100ml of Iohexol 350	80-100ml of Iohexol 350
Injection Rate	3-4ml/second	3-4ml/second	3ml/second
Scan Delay	Bolus tracking done	Bolus tracking	Bolus tracking
Pitch	0.9	0.75	0.8

3.11 Imaging Analysis

The images were analysed by the principal investigator and two experienced radiologists on the Picture Archiving and Communication Systems available at the imaging centres. The following MDCT imaging characteristics were evaluated: tumour multiplicity, size, location, shape, margins, homogeneity, presence of a capsule, internal architecture (whether solid, cystic or mixed solid and

cystic), size of largest cyst, cyst communication with pancreatic duct, presence of calcification, pre and post contrast attenuation characteristics, presence of secondary signs of malignancy (pancreatic and common bile duct abrupt cut off and dilatation, distal pancreatic atrophy, localised bulge in pancreatic contour), presence of a mural nodule within a pancreatic duct, adjacent structure invasion, lymph node involvement and presence of distant metastases(23,40,46,74,75,76). The most likely pancreatic tumour type was determined from the MDCT imaging characteristics by consensus and documented.

3.12 Histopathological analysis

The patients underwent either open biopsy during surgery or imaged guided percutaneous core biopsy. The time lapse between imaging and collection of histological specimens was three weeks on average. The histopathological evaluation was done at various facilites and the pathologists were blinded to the MDCT imaging diagnoses. Routine hematoxylin and eosin staining was done for all the samples and immunohistochemistry evaluation was included when necessary.

3.13 Data Variables

Table 3.2. Data variables

Objective	Variable	Categories
Prevalence of pancreatic tumour types	Histological diagnosis	
Demographic profile	Age	
	Sex	Male
		Female
Tumour characteristics MDCT imaging	Tumour multiplicity	Solitary
		Multifocal
		Diffuse infiltration
	Pancreatic location of tumour	Head
		Uncinate process
		Neck
		Body
		Tail
	Size of tumour (longest dimension in cm in any plane)	
	Tumour margins	Well circumscribed

		Partially circumscribed	
		Poorly circumscribed	
	Homogeneity	Homogenous	
		Heterogenous	
	Shape	Smooth	
		Lobulated	
		Irregular	
	Presence of a capsule	Present	
		Absent	
	Internal architecture	Solid	
		Cystic	
		Mixed solid and cystic	
	Septations	Present	
		Absent	
	Size of largest cyst (longest dimension in cm)		
	Attenuation characteristics (homogenous, heterogenous, hypovascular, hypervascular, rim enhancement)		
	Pre-contrast	Hypoattenuating	
		Hyperattenuating	
		Isoattenuating	
	Pancreatic phase	Homogenous	
		Heterogenous	
		Rim enhancement	
	Porto-venous phase	Homogenous	
		Heterogenous	
		Rim enhancement	
	Calcification	Present	Central
			Peripheral
		Absent	
	Localised bulge in pancreatic contour	Present	
		Absent	
	Abrupt pancreatic/biliary duct cut off	Present	
		Absent	
		Absent	
	Main pancreatic duct dilatation	Present	
		Absent	
	Common bile duct dilatation	Present	
		Absent	
	Double duct sign	Present	
		Absent	

	Distal pancreatic atrophy	Present	
		Absent	
	Mural nodule within a pancreatic duct	Present	
		Absent	
	Cyst communication with pancreatic duct	Present	
		Absent	
	Local invasion		
	Stomach	Present	
		Absent	
	Duodenum	Present	
		Absent	
	Spleen	Present	
		Absent	
	Bile duct	Present	
		Absent	
	Kidneys	Present	
		Absent	
	Vascular involvement (Hepatic artery, celiac trunk, SMA, Aorta, splenic artery, splenic vein, SMV, portal vein, IVC)	Abutment	
		Encasement	
		Calibre change	Present
			Absent
		Thrombosis	Present
			Absent
	Regional nodal involvement	Present	
		Absent	
	Distant metastasis	Present	
		Absent	
MDCT diagnostic accuracy	Likely tumour type from MDCT imaging findings	Pancreatic ductal adenocarcinoma	
		IPMN	MD-IPMN
			BD-IPMN
		SCN	
		MCN	
		Pancreatic lymphoma	
		Pancreatic neuroendocrine tumour	
		SPT	
		Secondary tumours	
		Pancreatoblastoma	
		Others	

	Histological diagnosis	Pancreatic ductal adenocarcinoma	
		IPMN	MD-IPMN
			BD-IPMN
		SCN	
		MCN	
		Pancreatic lymphoma	
		Pancreatic neuroendocrine tumour	
		SPT	
		Secondary tumours	
		Pancreatoblastoma	
		Others	

3.14 Data Collection Procedures

3.14.1 Data Capture Tool

A pre-designed data collection tool (appendix V) organised into sections with distinct groups of data that mirrored the study objectives was used. The first section captured demographic data including participant age and sex. The second section recorded the MDCT imaging pancreatic tumour characteristics. The third section was used to document the most likely imaging and the histopathological diagnoses, which were used to establish prevalence and MDCT diagnostic accuracy information.

3.14.2 Quality Assurance

The data collection tool was pre-tested before commencement of the study and necessary corrections were made to avoid ambiguity and misinterpretations. Two qualified radiologists apart from the principal investigator did the evaluation of MDCT imaging characteristics of the pancreatic tumours. Histopathological reports that differed from the pancreatic tumour subtype suggested by MDCT imaging were reviewed by a different experienced pathologist. Discrepant results after the review were further evaluated by a third pathologist as a tie-breaker. The re-evaluation was done using the original slides which were available.

3.14.3 Data Collection

Data collection commenced after ethical approval from KNH/UON ERC and obtaining permission from KNH, Plaza Imaging Solutions and German Medical Centre administration. Data was

collected after MDCT image evaluation and documented using the study collection tool (appendix V). The study participants were followed up to obtain the histopathological reports. For participants drawn from KNH, the reports were also sought from the medical records. The histopathological findings were also documented in the data collection tool.

3.15 Data Management and Analysis

Data was extracted from the abstraction tool, entered into a worksheet and analysis was done using the Statistical Package for Social Sciences software (SPSS). The distribution of continuous data was established using the Shapiro Wilks test. Demographic characteristics and the imaging characteristics of pancreatic tumors were summarised as means with standard deviations if continuous and as frequencies with percentages if categorical. Association between demographic characteristics and imaging characteristics were evaluated using the Chi square test and Student's t-test at 95% confidence level. For comparative analysies, probability values of <0.05 were statistically significant. The results were presented in tables, pie carts, and bar charts.

3.16 Ethical Considerations

3.16.1 Ethical Clearance and Confidentiality

Prior to commencement of the study, the proposal was presented to the KNH/UoN ERC for approval. Informed consent was obtained from all the eligible study participants. Participation was voluntary. Data was handled with utmost confidentiality through out the study period. All data collection tools were deidentified and study identification numbers were assigned to the study participants. A password protected computer was used for data entry and analysis.

3.17 Funding

The East Central Africa Division of the Seventh Day Adventist Church funded the study.

3.18 Study Results Dissemination Plan

The study findings have been presented to the Department of Imaging and Radiation Medicine at the University of Nairobi as part of the requirement of the postgraduate course. A written report

will be submitted to the department and to KNH-UoN ERC and Kenyatta National Hospital. The results will be published in a peer reviewed journal of Radiology**.**

3.19 Study Closure Plan and Procedure

Recruitment of participants and data collection stopped once the pre-determined minimum sample size of 39 had been attained.

CHAPTER 4 RESULTS

4.1 Demographic characteristics

Thirty-nine (39) participants met the criteria for inclusion. The distribution of ages ranged from 22 to 90 years. The mean age of the patients was 58.4±13.9 years. A majority were female (59.5%) and had an unknown history of extra-pancreatic malignancies (100%) (table 1).

Table 4.1. Demographic characteristics of patients with pancreatic tumours

Variable	Category	Frequency (N=39)
Age	Mean [SD]	58.4 [13.9]
Gender	Female	23(59.0)
	Male	16 (41.0)
Extra pancreatic malignancy	Known	0 (0.0)
	Unknown	39 (100)

4.2 Prevalence of pancreatic tumor subtypes

Four pancreatic tumor subtypes (pancreatic ductal carcinoma, pancreatic neuroendocrine tumor, solid pseudopapillary neoplasm and paraganglioma) were identified during histological analysis (figure 2). Two cases determined to be intraductal papillary mucinous neoplasm and pancreatic ductal adenocarcinoma on MDCT imaging were diagnosed as fat necrosis and normal pancreatic tissue respectively on histology. Pancreatic ductal carcinoma had the highest prevalence at 87.2%, while pancreatic neuroendocrine tumor, solid pseudopapillary neoplasm and paraganglioma constituted 2.6% each. The histological diagnoses of fat necrosis and normal pancreatic tissue also constituted 2.6% each. Other pancreatic tumor subtypes including intraductal papillary mucinous neoplasms, serous cystic neoplasms, mucinous cystic neoplasms, pancreatic lymphoma and secondary tumors were not detected on histological analysis.

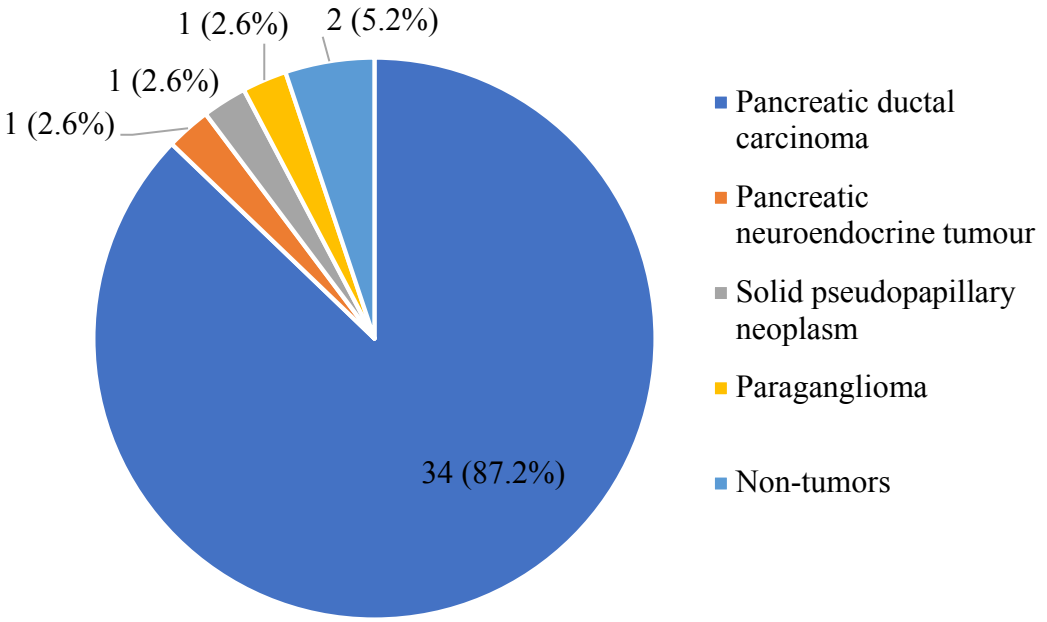


Figure 4.1. Prevalence of pancreatic tumor subtypes

4.3 Demographic profile of pancreatic tumors

4.3.1 Pancreatic ductal carcinoma

Patients with PDA were significantly older (60.6±10.6 years) than those without PDA (43.6±24.1 years), P=0.032. Females were 0.95 (CI 0.15-5.17) times less likely to have ductal carcinoma compared to males but the difference was not statistically significant (table 2).

Table 4.2. Demographic profile of patients with pancreatic ductal carcinoma

		Pancreatic ductal carcinoma			
		Present (N=34)	Absent (N=5)	OR (95% CI)	P value
Age	Mean±SD	60.6±10.6	43.6±24.1	-	0.032
Gender	Female	20 (87.0)	3 (13.0)	0.95 (0.15-5.17)	1.000
	Male	14 (87.5)	2 (12.5)	Reference	

4.4 Imaging characteristics of different pancreatic tumors

The MDCT imaging characteristics of pancreatic tumors identified after histological analysis presented in Figure 4.3 tables 4.3, 4.4, and 4.5.

4.4.1 Pancreatic tumour morphological characteristics

4.4.1.1 Pancreatic ductal carcinoma

All PDAs were solitary tumours (100%). Most were located in the pancreatic head (55.9%) with pancreatic body and tail tumours comprising 35.3% and 20.6% respectively (fig 3). The mean tumor size was 4.6±1.3with a range 2.4 - 7.6 cm. Most tumors were poorly circumscribed (91.2%), homogenous (67.6%), irregular (85.3%), and did not have a capsule (97.1%). Internal tumour architecture was mostly solid (85.3%). Cystic and mixed solid and cystic tumours comprised 5.9% and 8.8% of tumors. All PDAs with cystic components lacked communication with the main pancreatic duct (100%). The tumours were hypoattenuating on precontrast imaging in 55.5% of the cases and were hypovascular on pancreatic and portovenous phases in all cases (100% and 100%). Calcification was only seen in 8.8% of PDAs, and it occurred proportionally in diffuse, central, and peripheral locations when present (33.3% each). The commonest secondary signs seen were localised bulge in the pancreatic contour (73.5%), main pancreatic duct dilatation (61.8%) and distal pancreatic atrophy (58.8%). Abrupt biliary duct cut off, common bile duct dilatation, and mural nodule in a pancreatic duct were mostly absent (67.6%, 70.6%, 100%). Double duct sign was seen in 29.4% of the PDAs.

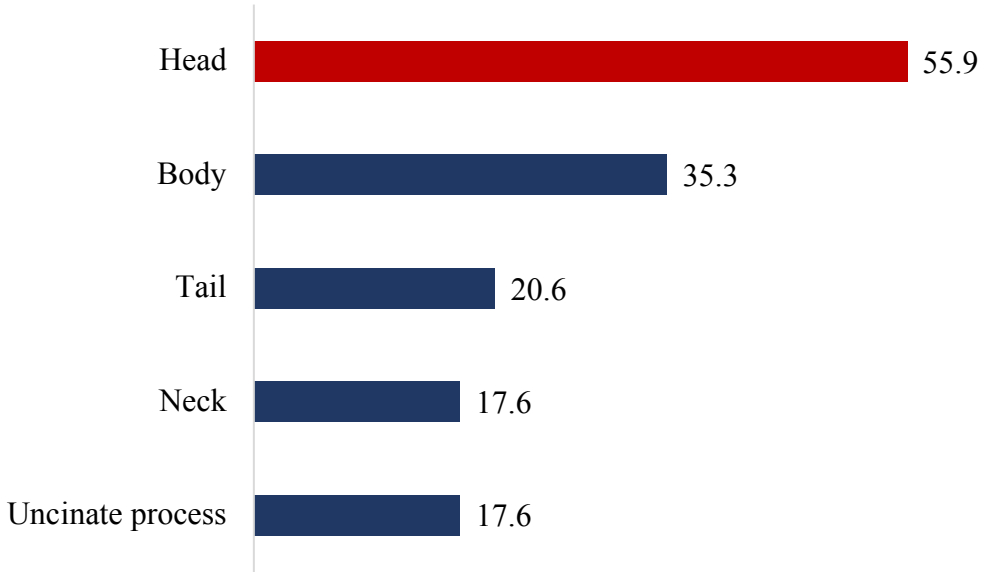


Figure 4.2. Pancreatic tumor location of PDAs

4.4.1.2 Pancreatic neuroendocrine tumor

On MDCT imaging, this was a solitary, poorly circumscribed, homogenous, solid tumour located in the neck and body of the pancreas. It measured 4cm, causing a localised bulge in the pancreatic contour. It was isoattenuating on precontrast imaging and was hypovascular on post contrast pancreatic and portovenous phases. There was distal pancreatic atrophy. No calcification was detected. The biliary and pancreatic ducts were of normal calibre with no abrupt cut off. This had been determined to be a PDA on MDCT imaging.

4.4.1.3 Solid Pseudopapillary Neoplasm

The appearance on imaging was a large, well circumscribed, encapsulated cystic mass with thin septations and solid mural nodules, located in the pancreatic body and tail. It measured 12.5cm. No calcifications were seen. The cystic components were non-enhancing, while the septations and mural nodules showed mild enhancement on post contrast arterial and portovenous phase imaging. There was mild distal pancreatic atrophy and MPD dilatation. No communication between the cystic components and the MPD was noted. This tumour was correctly identified as a SPN on MDCT imaging.

4.4.1.4 Paraganglioma

This was a 6.2-centimetre, solitary, well circumscribed, lobulated pancreatic body tumour that was predominantly solid on MDCT imaging. It was hypervascular on pancreatic and portovenous phases with central non-enhancing cystic degeneration. Calcification was absent. The pancreatic and biliary ducts were normal without distal pancreatic atrophy (table 4.3). On MDCT imaging, this tumour had been classified as a pancreatic neuroendocrine tumour.

Table 4.3. Pancreatic tumor morphological characteristics of pancreatic ductal carcinoma, pancreatic neuroendocrine tumor, paraganglioma, fat necrosis, and normal pancreatic tissue

		PDA N=34	PNET N=1	SPN N=1	Paraganglioma N=1	Fat necrosis N=1	Normal tissue N=1
Tumour multiplicity	Solitary	34 (100)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Location of tumor	Head	19 (55.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100)
	Body	12 (35.3)	1 (100)	1 (100)	1 (100)	1 (100)	0 (0.0)
	Tail	7 (20.6)	0 (0.0)	1 (100)	0 (0.0)	1 (100)	0 (0.0)
	Neck	6 (17.6)	1 (100)	0 (0.0)	0 (0.0)	1 (100)	0 (0.0)
	Uncinate process	6 (17.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100)
Size of tumor (cm)	Mean [SD]	4.6 (1.3)	4.4 (-)	12.5 (-)	6.2 (-)	10.1 (-)	3.6 (-)
Tumour margins	Partially circumscribed	2 (5.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Poorly circumscribed	31 (91.2)	1 (100)	0 (0.0)	0 (0.0)	1 (100)	1 (100)
	Well circumscribed	1 (2.9)	0 (0.0)	1 (100)	1 (100)	0 (0.0)	0 (0.0)
Homogeneity	Heterogenous	11 (32.4)	0 (0.0)	1 (100)	1 (100)	1 (100)	1 (100)
	Homogeneous	23 (67.6)	1 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Shape	Irregular	29 (85.3)	1 (100)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100)
	Lobulated	1 (2.9)	0 (0.0)	0 (0.0)	1 (100)	1 (100)	0 (0.0)
	Smooth	4 (11.8)	0 (0.0)	1 (100)	0 (0.0)	0 (0.0)	0 (0.0)
Capsule	Present	1 (2.9)	0 (0.0)	1 (100)	0 (0.0)	0 (0.0)	0 (0.0)
	Absent	33 (97.1)	1 (100)	0 (0.0)	1 (100)	1 (100)	1 (100)
Internal architecture	Solid	29 (85.3)	1 (100)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100)
	Cystic	2 (5.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Mixed	3 (8.8)	0 (0.0)	1 (100)	1 (100)	1 (100)	0 (0.0)
Architecture of cystic tumors							
Septations	Unilocular	2 (100)	-	0 (0.0)	0 (0.0)	0 (0.0)	-
	Multilocular	0 (0.0)	-	1 (100)	0 (0.0)	1 (100)	-
	Unknown	3					-
Communication with duct	Present	0 (0.0)	-	0 (0.0)	0 (0.0)	0 (0.0)	-
	Absent	5 (100)	-	1 (100)	1 (100)	1 (100)	-
Size of largest cyst	Microcystic	2 (50.0)	-	0 (0.0)	0 (0.0)	0 (0.0)	-
	Macrocystic	2 (50.0)	-	1 (100)	1 (100)	1 (100)	-

		PDA N=34	PNET N=1	SPN N=1	Paraganglioma N=1	Fat necrosis N=1	Normal tissue N=1
Precontrast	Hypoattenuating	19 (55.6)	0 (0.0)	1 (100)	-	1 (100)	0 (0.0)
	Isoattenuating	15 (44.1)	1 (100)	0 (0.0)	-	0 (0.0)	1 (100)
Pancreatic phase	Hypovascular	34 (100)	1 (100)	1 (100)	0 (0.0)	1 (100)	1 (100)
	Hypervascular	0 (0.0)	0 (0.0)	0 (0.0)	1 (100)	0 (0.0)	0 (0.0)
Portovenous phase	Hypovascular	34 (100)	1 (100)	1 (100)	0 (0.0)	1 (100)	1 (100)
	Hypervascular	0 (0.0)	0 (0.0)	0 (0.0)	1 (100)	0 (0.0)	0 (0.0)
Calcification	Present	3 (8.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Absent	31 (91.2)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Location of calcification	Diffuse	1 (33.3)	-	-	-	-	-
	Central	1 (33.3)	-	-	-	-	-
	Peripheral	1 (33.3)	-	-	-	-	-
Localised bulge in pancreatic contour	Present	25 (73.5)	1 (100)	1 (100)	0 (0.0)	1 (100)	1 (100)
	Absent	9 (26.5)	0 (0.0)	0 (0.0)	1 (100)	0 (0.0)	0 (0.0)
Abrupt pancreatic duct cut off	Present	23 (67.6)	0 (0.0)	1 (100)	0 (0.0)	1 (100)	1 (100)
	Absent	11 (32.4)	1 (100)	0 (0.0)	1 (100)	0 (0.0)	0 (0.0)
Abrupt biliary duct cut off	Present	11 (32.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100)
	Absent	23 (67.6)	1 (100)	1 (100)	1 (100)	1 (100)	0 (0.0)
Main pancreatic duct dilatation	Present	21 (61.8)	0 (0.0)	1 (100)	0 (0.0)	1 (100)	1 (100)
	Absent	13 (38.2)	1 (100)	0 (0.0)	1 (100)	0 (0.0)	0 (0.0)
Common bile duct dilatation	Present	10 (29.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100)
	Absent	24 (70.6)	1 (100)	1 (100)	1 (100)	1 (100)	0 (0.0)
Double duct sign	Present	10 (29.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100)
	Absent	24 (70.6)	1 (100)	1 (100)	1 (100)	1 (100)	0 (0.0)
Distal pancreatic atrophy	Present	20 (58.8)	1 (100)	1 (100)	0 (0.0)	0 (0.0)	0 (0.0)
	Absent	14 (41.2)	0 (0.0)	0 (0.0)	1 (100)	1 (100)	1 (100)
Mural nodule in a pancreatic duct	Present	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Absent	34 (100)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)

4.4.2 Tumour relationship with adjacent vascular structures

4.4.2.1 Pancreatic ductal carcinoma

Approximately 17.6% of PDAs had hepatic artery involvement, mostly as encasement (83.3%). About 23.5% had celiac trunk involvement, with 100% of them being encased and 12.5% having a calibre change. About 26.5% had SMA involvement, mostly encasement (66.7%), while 26.5% had SMV involvement, mostly encasement (77.8%). About 38.2%, 32.4%, and 5.9% had splenic vein, portal vein, and IVC involvement, mostly as thrombosis (61.5%), encasement (63.6%), and abutment (100%) respectively. Nine (26.5%) and 2 (5.9%) had splenic artery and abdominal aortic involvement respectively, mostly encasement (66.6%) and abutment (100%) respectively.

4.4.2.2 Pancreatic neuroendocrine tumor

There was encasement of hepatic artery, abutment of the celiac trunk and SMV, and thrombosis of the portal vein. The SMA, splenic vein, IVC, splenic artery, and the aorta were not involved.

4.4.2.3 Solid pseudopapillary neoplasm

All the adjacent vasculature were free of tumour.

4.4.2.4 Paraganglioma

The tumour showed abutment of the SMA. The other vessels were not involved (table 4.4).

Table 4.4. Tumour relationship with adjacent vascular structures

		PDA N=34	PNET N=1	SPN N=1	Paraganglioma N=1	Fat necrosis N=1	Normal tissue N=1
Involvement of hepatic artery	Present	6 (17.6)	1 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Encasement	5 (83.3)	1 (100)	-	-	-	-
	Abutment	1 (16.7)	0 (0.0)	-	-	-	-
	Absent	28 (84.8)	0 (0.0)	1 (100)	1 (100)	1 (100)	1 (100)
Involvement of celiac trunk	Present	8 (23.5)	1 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Encasement	8 (100)	0 (0.0)	-	-	-	-
	Caliber change	1 (12.5)	1 (100)	-	-	-	-
	Absent	26 (78.8)	0 (0.0)	1 (100)	1 (100)	1 (100)	1 (100)
Involvement of SMA	Present	9 (26.5)	0 (0.0)	0 (0.0)	1 (100)	0 (0.0)	0 (0.0)
	Encasement	6 (66.7)	-	-	0 (0.0)	-	-
	Abutment	3 (33.3)	-	-	1 (100)	-	-
	Calibre change	2 (22.2)	-	-	0 (0.0)	-	-
	Absent	25 (75.8)	1 (100)	1 (100)	0 (0.0)	1 (100)	1 (100)
Involvement of SMV	Present	9 (26.5)	1 (100)	0 (0.0)	0 (0.0)	1 (100)	1 (100)
	Encasement	7 (77.8)	1 (100)	-	-	0 (0.0)	0 (0.0)
	Abutment	2 (22.2)	0 (0.0)	-	-	0 (0.0)	1 (100)
	Calibre change	2 (22.2)	0 (0.0)	-	-	0 (0.0)	0 (0.0)
	Thrombosis	1 (11.1)	1 (100)	-	-	1 (100)	0 (0.0)
	Absent	24 (72.7)	0 (0.0)	1 (100)	1 (100)	0 (0.0)	0 (0.0)
Involvement of splenic vein	Present	13 (38.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100)	0 (0.0)
	Encasement	6 (46.2)	-	-	-	0 (0.0)	-
	Abutment	2 (15.4)	-	-	-	0 (0.0)	-
	Calibre change	2 (15.4)	-	-	-	0 (0.0)	-
	Thrombosis	8 (61.5)	-	-	-	1 (100)	-
	Absent	21 (63.6)	1 (100)	1 (100)	1 (100)	0 (0.0)	1 (100)
Involvement of portal vein	Present	11 (32.4)	1 (100)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100)
	Encasement	7 (63.6)	0 (0.0)	-	-	-	0 (0.0)
	Abutment	2 (18.2)	0 (0.0)	-	-	-	1 (100)
	Calibre change	4 (36.4)	0 (0.0)	-	-	-	0 (0.0)
	Thrombosis	2 (18.2)	1 (100)	-	-	-	0 (0.0)
	Absent	22 (66.7)	0 (0.0)	1 (100)	1 (100)	1 (100)	0 (0.0)

		PDA N=34	PNET N=1	SPN N=1	Paraganglioma N=1	Fat necrosis N=1	Normal tissue N=1
Involvement of IVC	Present	2 (5.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Abutment	2 (100)	-	-	-	-	-
	Absent	31 (93.9)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Involvement of Splenic artery	Present	9 (26.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Encasement	6 (66.6)	-	-	-	-	-
	Abutment	3 (33.3)	-	-	-	-	-
	Thrombosis	1 (11.1)	-	-	-	-	-
	Absent	25 (75.8)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Involvement of Aorta	Present	2 (5.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Abutment	2 (100)	--	-	-	-	-
	Absent	32 (94.1)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)

4.4.3 Local and distant tumour spread

4.4.3.1 Pancreatic ductal carcinoma

Local invasion of the duodenum (26.5%), stomach, spleen, kidney, jejunum, and adrenal gland (2.9% each) was observed. Most of the PDAs had regional lymph node involvement (55.9%). Distant metastases were present in 47.1% of the cases.

4.4.3.2 Pancreatic neuroendocrine tumor

Locoregional involvement and distant metastases were absent.

4.4.3.3 Solid pseudopapillary neoplasm

Locoregional involvement and distant metastases were absent.

4.4.3.4 Paraganglioma

Locoregional involvement and distant metastases were absent (table 4.5).

Table 4.5. Local and distant tumour spread

		PDA N=34	PNET N=1	SPN N=1	Paraganglioma N=1	Fat necrosis N=1	Normal tissue N=1
Local invasion of stomach	Present	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Absent	33 (97.1)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Local invasion of duodenum	Present	9 (26.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Absent	25 (73.5)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Local invasion of spleen	Present	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Absent	33 (97.1)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Local invasion of bile duct	Present	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Absent	34 (100)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Local invasion of kidneys	Present	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Absent	33 (97.1)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Local invasion of jejunal	Present	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Absent	33 (97.1)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Local invasion of adrenal	Present	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Absent	33 (97.1)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Regional nodal involvement	Present	19 (55.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100)	0 (0.0)
	Absent	15 (44.1)	1 (100)	1 (100)	1 (100)	0 (0.0)	1 (100)
Distant metastasis	Present	16 (47.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Absent	18 (52.9)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)

4.5 Diagnostic accuracy of MDCT imaging with histopathological diagnosis as the reference standard.

4.5.1 Pancreatic ductal carcinoma

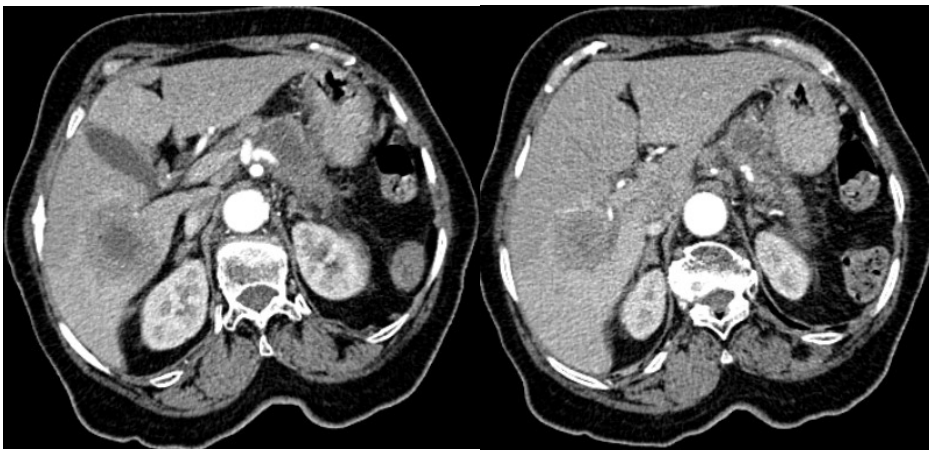
The diagnostic accuracy of MDCT imaging for PDA was 94.9%. Sensitivity and specificity were 100% and 60% respectively, while the PPV and NPV were 94.4% and 100%.

Table 4.6. Diagnostic accuracy of MDCT imaging for pancreatic ductal carcinoma

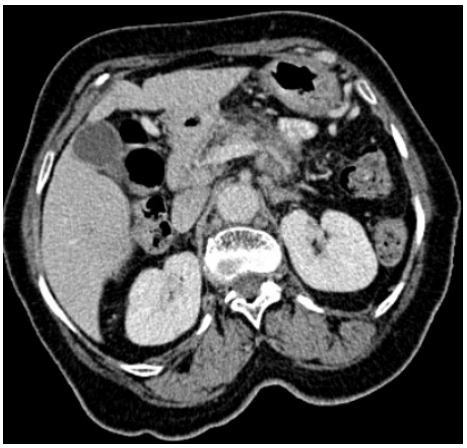
		Histology (Standard Reference)	
		Positive [N=34]	Negative [N=5]
MDCT (Index Test)	Positive [N=36]	34	2
	Negative[N=3]	0	3

4.6 Description of select imaging findings

Case 1:



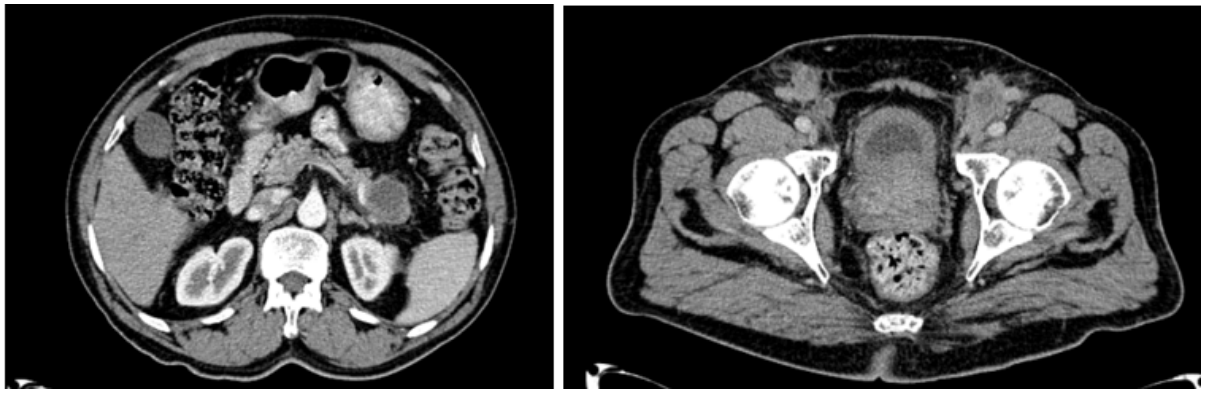
a **b**



c

Figure 4.3. A 90-year-old female with pancreatic ductal adenocarcinoma. Axial CECT images of the abdomen in arterial and portovenous phases. a) A poorly circumscribed hypovascular pancreatic body mass encasing the splenic artery. An ill-defined hypovascular metastatic mass with a necrotic centre is seen in segment v of the liver. b) The pancreatic tail is atrophic with mild prominence of the pancreatic duct. c) The splenic vein is also encased by the mass.

Case 2:



a **b**

Figure 4.4. A seventy-two-year-old male who presented with inguinal adenopathy. Histological evaluation after biopsy of the nodes revealed metastatic disease. CT abdomen and chest were done in search of the primary tumour. a) Axial CECT in arterial phase shows a well defined, cystic pancreatic tail mass with adjacent fat stranding. b) Axial CECT in portovenous phase demonstrates bilateral inguinal adenopathy with central necrosis. The pancreatic tumour was diagnosed to be a pancreatic ductal adenocarcinoma on histopathology.

Case 3:

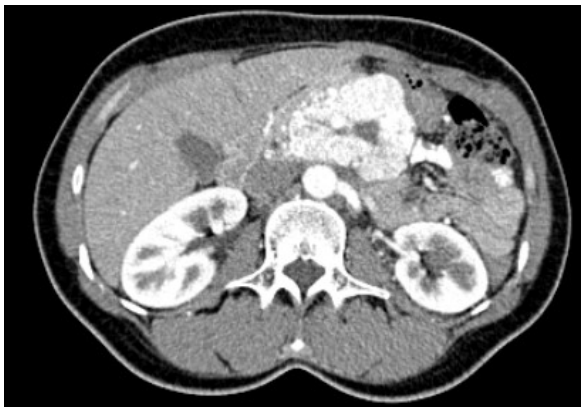
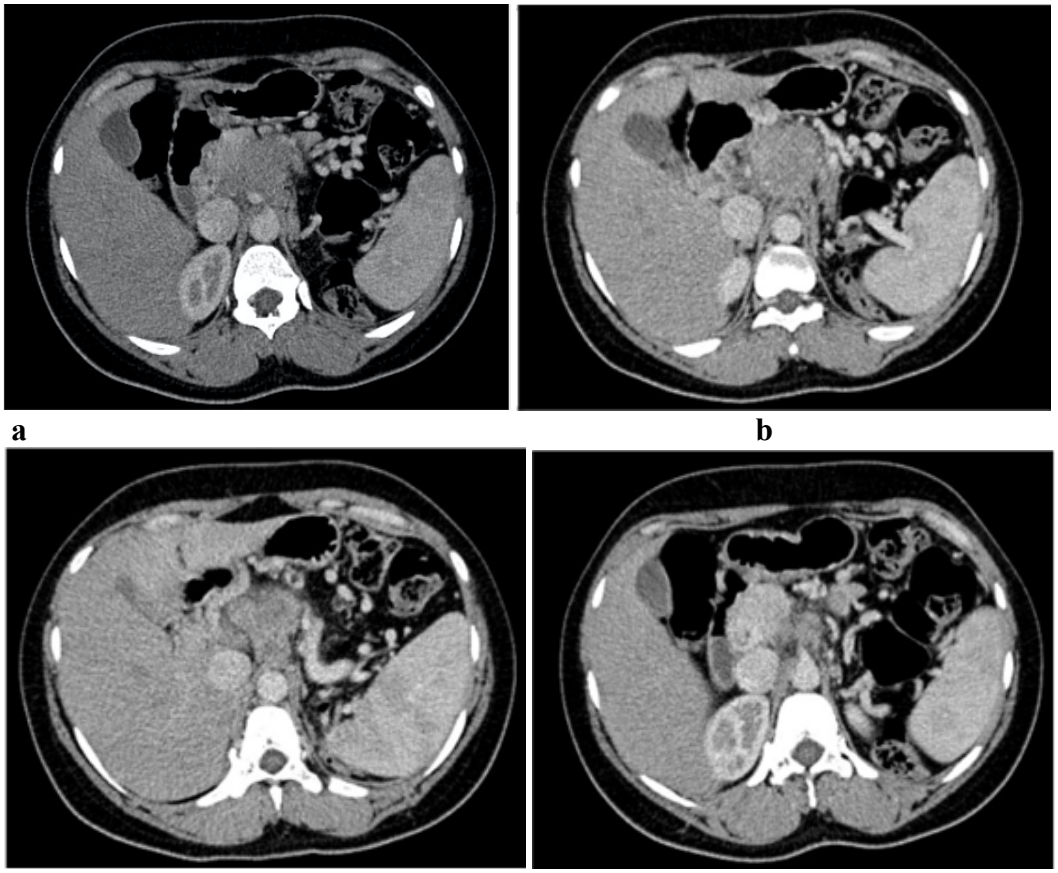


Figure 4.5. Thirty-six-year-old female with a pancreatic paraganglioma. Axial CECT in arterial phase showing a large, well circumscribed lobulated tumour in the pancreatic head and neck that was hypervascular relative to the normal pancreatic parenchyma.

Case 4:

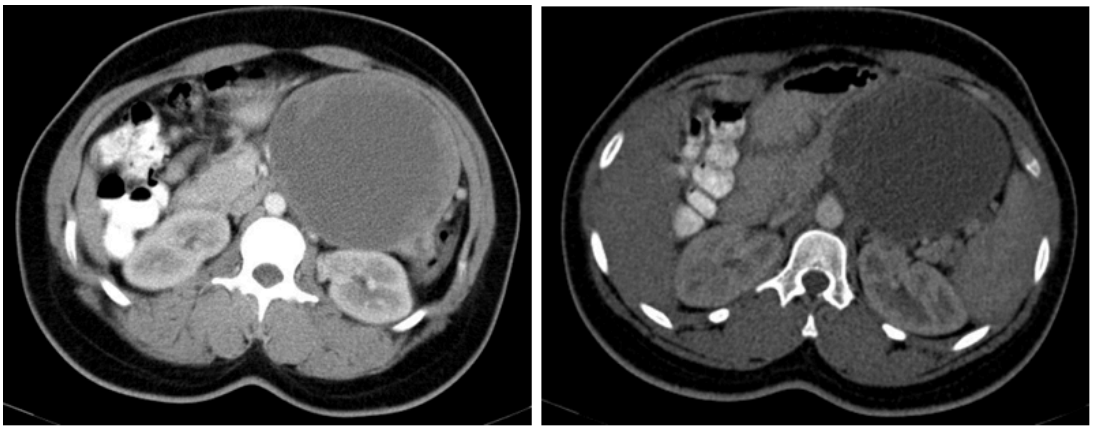


a **b**

c **d**

Figure 4.6. A forty-one-year-old female with PNET. Axial CECT images of the abdomen in late arterial phase. a) There is a poorly circumscribed hypoenhancing solid pancreatic neck tumour. The tumour abuts the celiac artery. B) It encases and narrows the common hepatic artery. c) At an image that is at a higher level the pancreatic body and tail are not visualised due to atrophy. d) The pancreatic head is seen to be normally enhancing with a normal calibre distal common bile duct.

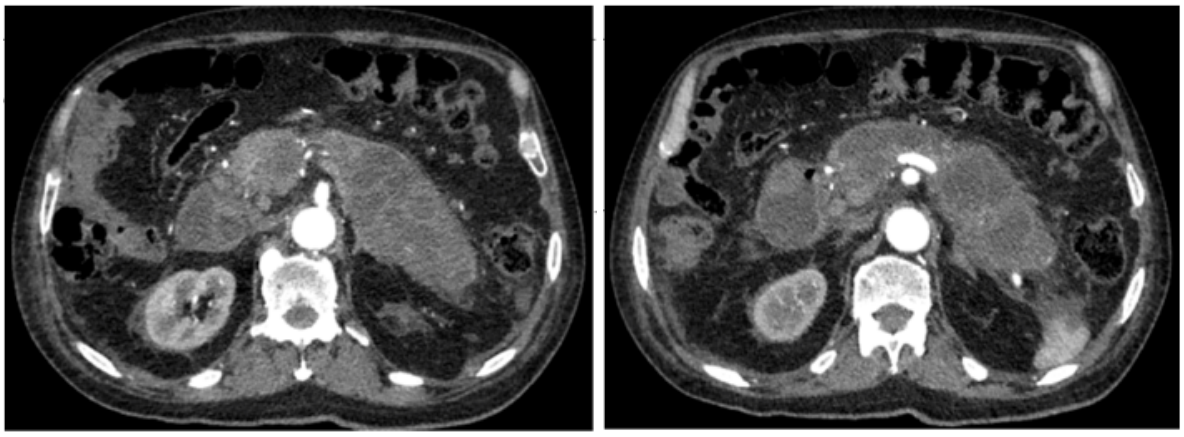
Case 5



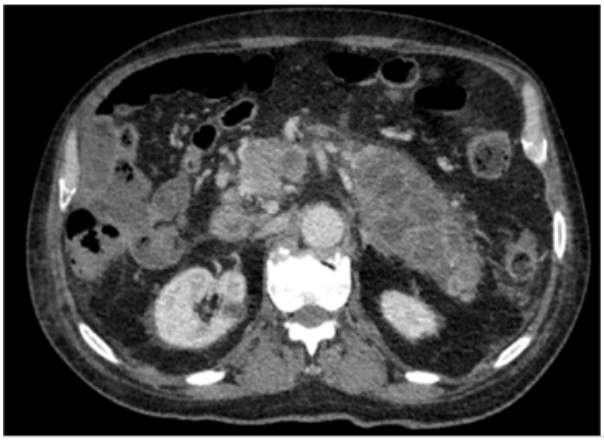
a **b**

Figure 4.7. Twenty-two-year-old female patient with SPN. Axial CECT images in arterial phase. a) A large, well circumscribed, multiloculatedencapsulated cystic mass with solid mural nodules is seen in the pancreatic body and tail. b) Windowing done to show fine septations within the cystic mass.

Case 6:



a **b**



c

Figure 4.8. An eighty-five-year-old male with fat necrosis on histopathology. a) Axial CECT in arterial phase show an enlarged pancreatic body and tail which are replaced by a poorly circumscribed, multiloculated hypoenhancing cystic lesion. b) Main pancreatic duct dilatation is seen at the pancreatic neck and body regions. There is associated mild peripancreatic fat stranding. c) Axial portovenous phase CECT image demonstrates a filling defect in the superior mesenteric vein indicative of thrombosis.

CHAPTER 5 DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

5.1 Discussion

In this study conducted among patients found to have pancreatic tumours on MDCT evaluation at three imaging centres in Nairobi, Kenya we found that pancreatic ductal adenocarcinoma was the most prevalent at 87.2% which is consistent to what has been reported in literature. PDAs are the most commonly occurring pancreatic tumours comprising between 80 and 90% of pancreatic tumours (77,78).

Patients with PDA had a mean age of 60.6± 10.6 years. This was comparable to findings in Korea and Romania by Kim et al, 2010 and Costache et al, 2016 respectively of 60 years and 64 years respectively (15,16). In the current study, there was a 58.8% female predilection for PDA which differed with 61% and 60.9% male predilection reported by Costache et al and Kim et al respectively (15,16). Sellam et al, 2015 from North Africa also reported 65.6% male preponderance (17). The higher female frequency in our study could be a reflection of difference in health seeking behaviour by the different sexes in our region.

Most of the PDAs in the current study were located in the pancreatic head (55.9%). Other investigaters have also reported PDA predilection for the pancreatic head ranging from 56 to 70%(15,18,79). The mean tumour size was 4.6±1.3cm which is larger than 3cm reported by Costache et al and 2.65cm by Lee et al, 2008 (81). The relatively larger tumour size in the current study could be attributed to late presentation either due to health seeking behaviour or delays occasioned by the covid pandemic.

All the PDAs in our study were hypovascular during the pancreatic and portovenous phases. A meta-analysis carried out by Shirkhande et al in India in 2012 however noted that upto 11% of pancreatic carcinomas were isoattenuating (1). According to Kim et al, isoattenuating tumours comprised 5.4% of 644 pancreatic ductal adenocarcinomas (16). The presence of these isoattenuating tumours in these previous studies was inferred by the presence of secondary signs like pancreatic and common bile duct dilatation, atrophy of the distal pancreatic parenchyma, focal pancreatic contour bulge, presence of retention cysts within the pancreas and a focal area of fat sparing in a pancreas with fatty change. Yoon et al, 2011 reported that isoattenuating tumours were commoner in smaller tumours of less than 20mm diameter than

in larger tumours of 20-30mm, a finding that was statistically significant (P= 0.033) (18). They were also commoner in well differentiated than in moderately and poorly differentiated tumours. The tumours in our study were comparatively larger than in other studies and we hypothesize that to be the reason why none was found to be iso-attenuating.

In our study, 47.1% of patients with PDAs had distant metastases, 17.6% had encasement of the SMA, 23.5% had celiac axis encasement and 5.9% had aortic invasion (specifically abutment). These represent patients with unresectable disease according to the National Comprehensive Cancer Network (NCCN) unresectability guidelines. A study done in Saudi Arabia reported comparable findings of 40.5% of patients with PDA having distant metastases(82). Khattab et al, 2012 found 76.2% of PDAs to have distant metastases, with 14.3% showing encasement of the SMA in a study conducted in Egypt (83).

MDCT imaging diagnostic accuracy determined for PDA in the current study was 94.9% with sensitivity and specificity of 100% and 60%, and PPV and NPV of 94.4% and 100% respectively. Shirkhande et al in India reported MDCT sensitivity and specificity of 75 to 100% and 70 to 100% respectively in the diagnosis of pancreatic carcinomas(1). The sensitivity in the meta-analysis was higher (98%) for tumours exceeding 2cm in size. Costache et al determined that MDCT had a diagnostic accuracy of 83.3%, sensitivity and specificity of 81.4% and 43%, PPV and NPV of 61.5% and 56.7% respectively with higher accuracy for tumours greater than 20mm in size. All the patients in our study had tumours that were larger than 2cm in size which could account for the slightly higher measures of diagnostic accuracy. MDCT accuracy in the diagnosis of pancreatic tumour subtypes may be affected by overlap of imaging characteristics among different tumour subtypes. Hypovascular PNETS for example may mimic pancreatic ductal adenocarcinomas. Presence of inflammation as may occur in mass forming pancreatitis may also be a confounder in the diagnostic accuracy tests.

One pancreatic paraganglioma was encountered in our study. On MDCT imaging it was a well circumscribed solid pancreatic body tumour that was hypervascular on pancreatic and portovenous phases with central cystic degeneration. Pancreatic paragangliomas are very rare and fewer than 30 cases have been reported in literature(84). Our MDCT imaging findings for the one pancreatic paraganglioma encountered were similar to what has been reported in literature. Manning et al has described pancreatic paragangliomas to be well defined hyperenhancing solid tumours with cystic areas (85).

A twenty-two-year-old female patient was found to have a solid pseudopapillary neoplasm that was a 12.5cm, well circumscribed, encapsulated cystic tumour with solid mural nodules and septations. There was mild pancreatic duct dilatation. The findings in this patient mirror what has been documented in literature. SPNs are reported to comprise 2%-3% of pancreatic neoplasms (45). They have a female preponderance, and commonly occur in the third and fourth decades of life (46,47,48). A study done by Raman et al in the United States of America reported SPNs to be large (mean 5.34cm), well defined, encapsulated tumours, ranging from entirely cystic to entirely solid, with upto 46.7% having calcifications. There was no pancreatic nor biliary duct dilatation. They showed almost even distribution between the pancreatic head, body and tail (30%, 30%, 40%) (46). Anil et al, 2017 from Singapore found that 80% of SPNs were mixed cystic and solid, 50% were encapsulated, 40.5% had calcifications and all the tumours were hypoenhancing on post contrast imaging. Those that were located in the tail had a mean diameter of 12.6cm. Smaller tumours measuring about 3cm in size were however purely solid (49). A Chinese study by Yu P-F et al reported a mean tumour size of 7.87cm, with 60.12% of SPNs, being mixed cystic and solid (47).

A pancreatic neuroendocrine tumour was found in this study. It was a poorly circumscribed, homogenous, solid pancreatic neck and body tumour that was hypovascular on pancreatic and portovenous phases. The majority of PNETs are hypervascular tumours. Gusmini et al reported 17% of PNETs to be hypovascular in a study conducted in Italy (42). Karmazanovsky et al from Russia reported 41.9% of PNETs to be non hypervascular, and MDCT findings that were most predictive of a non hypervascular PNET were the absence pancreatic duct ectasia and absence of peripancreatic infiltration(86). The pancreatic duct was of normal calibre in our case and locoregional involvement and distant metastases were absent.

Study limitations included loss of some potential study participants due to death or financial constraints. Some of the pancreatic tumour subtypes are uncommon and hence adequate numbers were not achieved during the study. Statistical analysis for MDCT imaging findings and diagnostic accuracy tests was not done for the PNET, SPN and paraganglioma since they were under represented in this study.

5.2 Conclusion

The study has shown that pancreatic ductal adenocarcinoma is the most prevalent of the pancreatic tumour subtypes in Kenya. MDCT imaging using the pancreatic protocol had high

accuracy comparable to studies conducted elsewhere and is reliable in the diagnosis and exclusion of pancreatic ductal adenocarcinoma.

5.3 Recommendations

We recommend larger multicentre studies to evaluate the less commonly occurring pancreatic tumour subtypes. Retrospective studies focusing on the less common subtypes can be done to determine MDCT imaging features and diagnostic accuracy.

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APPENDICES

Appendix I: WHO Classification of Tumours of the Pancreas

Epithelial tumours

Benign

- Acinar cell cystadenoma
- Serous cystadenoma

Premalignant lesions

- Pancreatic intraepithelial neoplasia, grade 3 (PanIN-3)
- Intraductal papillary mucinous neoplasm with low- or intermediate-grade dysplasia
- Intraductal papillary mucinous neoplasm with high-grade dysplasia
- Intraductal tubulopapillary neoplasm
- Mucinous cystic neoplasm with low- or intermediate-grade dysplasia
- Mucinous cystic neoplasm with high-grade dysplasia

Malignant

Ductal adenocarcinoma

- Adenosquamous carcinoma
- Colloid carcinoma (mucinous non-cystic carcinoma)
- Hepatoid carcinoma
- Medullary carcinoma
- Signet ring cell carcinoma
- Undifferentiated carcinoma
- Undifferentiated carcinoma with osteoclast-like giant cells
- Acinar cell carcinoma
- Acinar cell cystadenocarcinoma
- Intraductal papillary mucinous neoplasm with an associated invasive carcinoma
- Mixed acinar-ductal carcinoma
- Mixed acinar-neuroendocrine carcinoma
- Mixed acinar-neuroendocrine-ductal carcinoma
- Mixed ductal-neuroendocrine carcinoma
- Mucinous cystic neoplasm with an associated invasive carcinoma
- Pancreatoblastoma
- Serous cystadenocarcinoma
- Solid-pseudopapillary neoplasm

Neuroendocrine neoplasms

- Pancreatic neuroendocrine microadenoma
- Neuroendocrine tumour (NET)
  - Non-functional pancreatic NET, G1, G2
  - NET G1
  - NET G2
- Neuroendocrine carcinoma (NEC)
  - Large cell NEC
  - Small cell NEC
- EC cell, serotonin-producing NET (carcinoid)
- Gastrinoma
- Glucagonoma
- Insulinoma
- Somatostatinoma
- VIPoma

Mature teratoma

Mesenchymal tumours

Lymphomas

Secondary tumours

Appendix II (a): Consent form (English)

PARTICIPANT INFORMATION AND CONSENT FORM

Title of Study:

PANCREATIC TUMORS: A MULTICENTRE STUDY OF MULTIDETECTOR COMPUTED TOMOGRAPHY FINDINGS AND HISTOPATHOLOGIC CORRELATION IN NAIROBI, KENYA.

Principal Investigator and institutional affiliation:

Dr. Roseline Kerubo Ogaro, Department of Imaging and Radiation medicine, University of Nairobi.

Introduction:

I would like to tell you about a scientific study being conducted by the above listed researcher. This consent form will provide you with the information you need to help you decide whether or not to be a participant in the study. Feel free to ask any questions about the purpose of the research, the possible risks and benefits, your rights as a volunteer, and anything else about the study or this form that you do not understand. When you are satisfied with the information given to you, you may make the decision whether you will be a participant in the study or not. This process is called 'informed consent'. If you agree to be in the study, I will request you to sign your name on this form. You should understand the following:

i) Your decision to participate is entirely voluntary
ii) You may withdraw from the study at any point in time without having to give a reason.
iii) Refusal to participate in the research or withdrawal will not affect the services you are entitled to in this health facility or any other facilities.
iv) You will receive a copy of this form for your record.

May I continue? YES / NO

This study has approval by The Kenyatta National Hospital-University of Nairobi Ethics and Research Committee protocol No. _____

WHAT IS THIS STUDY ABOUT?

The researcher listed above is recruiting individuals who are found to have tumours of the pancreas on computed tomography (CT scan) imaging. The CT scan findings will be analysed and compared to the histopathology reports. Histopathology reports refers to the laboratory results obtained after analysis of tissue samples obtained from the tumours after biopsy or surgery. The purpose of the study is to expand knowledge about the different pancreatic tumour types that occur in Kenyan patients. There will be at least 39 participants in this study. We are asking for your consent to consider participating in the study.

WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH STUDY?

Even before you are enrolled into the study, your primary doctor will have already requested for you to have an abdominal CT scan to further evaluate your illness. The researchers will have access to and will analyse your CT images.

The principal investigator or a research assistant may obtain information from your medical records pertaining your histopathological report. They may also seek you out to provide the histopathological report if this cannot be obtained from your medical records.

These results will be compared to the findings that will be obtained from your CT images.

We will ask for a telephone number where we can contact you if necessary. If you agree to provide your contact information, it will be used only by people working for this study and will never be shared with others. We may need to contact you to provide your histopathological report.

ARE THERE ANY RISKS, HARMS DISCOMFORTS ASSOCIATED WITH THIS STUDY?

One potential risk of participating in this study is loss of confidentiality. All effort shall be put in place to minimize the possible risk. All information obtained from you, your medical records or CT images will be treated with utmost confidentiality. Your name and hospital identification numbers will not appear in the data collection tools and the final report of the study. A code number will be used instead for identification purposes in a password-protected computer database. All paper records will be stored in a locked file cabinet. However, no system of protecting your confidentiality can be absolutely fool proof and so it is still possible that someone could find out you were in this study and could access information about you.

ARE THERE ANY BENEFITS OF BEING IN THIS STUDY?

Information obtained from this study will help health care givers to better understand the different types of pancreatic tumours that occur in Kenya. It will be a contribution to science and will help to improve promptness and accuracy of diagnosis of pancreatic tumours.

WILL BEING IN THIS STUDY COST YOU ANYTHING?

The study will not cost you any extra money. The CT imaging, any surgery or biopsy you may have will have been recommended by your primary doctor as part your disease evaluation or management.

WILL YOU GET A REFUND FOR ANY MONEY SPENT AS PART OF THIS STUDY?

We do not anticipate that you will use your money to facilitate the study. We will contact and meet you when need arises and we will bear the costs of this. Therefore, there will be no need for a refund.

WHAT IF YOU HAVE QUESTIONS IN FUTURE?

If you have any queries about the study, feel free to contact the study staff on the numbers provided below.

For more information about your rights as a research participant you may get in touch with the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 Ext. 44102, email uonknh_erc@uonbi.ac.ke.

The study staff will pay you back for telephone charges incurred if the call is for study related communication.

WHAT ARE YOUR OTHER CHOICES?

Your decision to participate in this research is voluntary. You are free to decline participation in the study and can decide to withdraw from the study at any time. This will not have any consequences on the treatment for your illness.

CONSENT FORM (STATEMENT OF CONSENT)

Participant's statement

I have read this consent form or had the information read to me and I have discussed this research study with a study staff. My questions have been answered in a language that I understand. The risks and benefits have been explained to me. I understand that participation in this study is voluntary and that I may decide to withdraw at any point in time. I freely agree to participate in this research study.

I understand that all efforts will be made to safeguard my confidentiality.

By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study.

I agree to participate in this research study:

Yes / No

I agree to avail the histopathological report if required.

Yes / No

I agree to provide contact information for follow-up.

Yes / No

Participant printed name: _____

Participant signature / Thumb stamp _____

Date _____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this study to the participant named above. I believe that the participant has understood and has voluntarily given his/her consent.

Researcher's Name: _____

Signature: _____

Date: _____

Role in the study: _____ [i.e. study staff who explained informed consent form.]

For more information contact Dr. Roseline Kerubo Ogaro on 0705240278 from 9.00 AM to 4.00 PM.

Witness Printed Name (If necessary): _____

Contact information: _____

Signature /Thumb stamp: _____

Date: _____

Appendix II (b): Consent form (Swahili)

FOMU YA MAELEZO NA IDHINI YA KUSHIRIKI KATIKA UTAFITI.

Mada la utafiti:

UVIMBE ZA KONGOSHO: UCHAMBUZI WA MATOKEO YA PICHA YA CT SCAN IKILINGANISHWA NA RIPOTI YA HISTOPATHOLOJIA KATIKA VITUO VITATU MJINI NAIROBI, KENYA.

Mtafiti Mkuu:

Dkt. Roseline Kerubo Ogaro, Idara ya Radiolojia, Chuo Kikuu cha Nairobi.

Utangulizi:

Ningependa kukujulisha juu ya utafiti huu unaohusiana na uvimbe za kongosho ili upate kuwa na habari itakayokusaidia kuamua kama utashiriki kwenye utafiti au la. Una uhuru wa kuuliza swali lolote kuhusiana na utafiti kama vile manufaa au madhara unaweza pata kutokana na utafiti, haki zako au swali lolote lile. Ukishapata majibu yote ya maswali utakayokuwa nayo, unaweza amua kama utashiriki au la. Ukikubali kushiriki, utatia sahihi kwenye fomu hii.

Mambo haya matatu ni muhimu:

1. Kushiriki kwako kwenye utafiti ni kwa hiari yako.
2. Unaweza jiondoa kwenye utafiti wakati wowote bila kuhitajika kupeana sababu.
3. Ukiamua kutoshiriki au kujiondoa baadaye hakutakuwa na athari zozote na bado utapata matibabu vile unvyostahili.

Ninaweza endelea? Ndio / Hapana

Utafiti huu umeidhinishwa na Kamati ya Maadili na Utafiti ya hospitali kuu la Kenyatta na Chuo Kikuu cha Nairobi; nambari ya itifaki: _____.

Utafiti unahusu nini?

Utafiti huu utashirikisha wagonjwa ambao watapatikana kuwa na uvimbe kwenye kongosho baada ya kufanyiwa picha ya CT scan. Matokeo ya picha yatachambuliwa na kulinganishwa na matokeo ya histolojia. Matokeo ya histolojia hupatikana baada ya sehemu ndogo kwenye uvimbe kutolewa ili ichunguzwe kwenye maabara.

Utafiti huu unanuia kuongeza maarifa zaidi kuhusu aina mbali mbali za uvimbe zinazotokea kwenye kongosho humu nchini Kenya.

Kutakuwa na jumla ya washiriki wasiopungua thelathini na tisa katika utafiti huu. Tungependa upeane idhini kushiriki.

Mambo yapi yatafanyika ukiamua kushiriki kwenye utafiti?

Hata kabla ya kushiriki, daktari wako atakuwa amependekeza ufanyiwe picha ya CT scan. Watafiti hawa wataweza kupata matokeo hayo na kuona picha zenyewe. Mtafiti mkuu au msaidizi atakagua rekodi zako za matibabu kupata ripoti ya histolojia. Huenda pia watawasiliana nawe ili kupata ripoti ya histolojia ikiwa habari hiyo haitapatikana kutoka kwa rekodi zako za matibabu.

Tutahitaji utupe nambari yako ya simu ili tuweze kuwasiliana na wewe. Nambari hiyo itatumika na watu wanaofanya utafiti huu pekee na haitapeanwa kwa watu wengine. Tutahitaji kuwasiliana na wewe ili tuweze kupata ripoti ya histolojia.

Kutakuwa na athari zozote kuhusiana na utafiti?

Kuna uwezekano wa kupoteza usiri wako ukishiriki kwenye utafiti huu. Tutaweka juhudi zote ziwezekanazo ili isifanyike. Taarifa yote kutoka kwako, kutoka kwa rekodi za matibabu na matokeo ya picha itawekwa siri. Majina, nambari zako za hospitali na taarifa yoyote ya kukutambulisha haitawekwa kwenye ripoti ya utafiti huu. Nambari maalum itatumika badala ya jina lako na nambari yako ya hospitali. Kompyuta itakayotumika itakuwa na nywila ili kuzuia watu wasiokuwa na idhini kupata habari yako. Makaratasi yote yatakayotumika yatawekwa kwenye kabati linalofungwa na kifunguu. Walakini, hata tukichukua hatua zote ziwezekanazo, kuna uwezekano kuwa mtu asiye na idhini bado ataweza kupata taarifa kukuhusu.

Kutakuwa na faida yoyote katika kushiriki kwenye utafiti?

Kushiriki itakuwa ni changio kwa ufahamu wa sayansi. Maarifa yatakayotokana na utafiti huu yataboresha utambuzi wa aina mbali mbali za uvimbe za kongosho kwa haraka na usahihi miongoni mwa madaktari nchini Kenya.

Kushiriki itakugharimu chochote?

Utafiti huu hautakugharimu pesa ziada kwani picha ya CT scan na uchunguzi wa histolojia zitakuwa zimependekezwa na daktari wako wa kibinafsi ili aweze kutambua ugonjwa wako.

Utarudishiwa pesa yoyote utakayotumia kwenye utafiti?

Kwa sababu hakuna pesa zaidi utagharimika, hakuna pesa utakayorudishiwa. Tutakapohitajika kuwasiliana au kukutana nawe, sisi wenyewe tutafanya hivyo na gharama itakuwa kwetu sisi.

Na je ukiwa na maswali yoyote siku za usoni?
Ukiwa na swali lolote kuhusu utafiti huu, unaweza kuwasiliana na Dkt. Roseline Kerubo Ogaro kupitia namba ya rununu 0705240278 kutoka saa tatu asubuhi, hadi saa kumi alasiri.

Ukihitaji habari zaidi kuhusu haki yako kama mshiriki kwenye utafiti unaweza pia kuwasiliana na karani / mwenyekiti, Kamati ya Maadili na Utafiti ya hospitali kuu ya Kenyatta / Chuo Kikuu cha Nairobi kupitia nambari ya simu: (020) 2726300 Ext 44102, barua pepe: uonknh_erc@uonbi.ac.ke.

Wafanyikazi wa utafiti watakurudishia pesa utakayotumia kupiga simu ikiwa unapiga kuhusiana na utafiti huu.

Una chaguo lingine?
Uamuzi wa kushiriki kwenye utafiti ni kwa hiari yako. Una uhuru wa kutoshiriki na unaweza pia amua kujiondoa kwenye utafiti wakati wowote. Kujiondoa hakutasababisha mabadiliko yoyote kwenye matibabu yako.

FOMU YA IDHINI
TANGAZO LA MSHIRIKI
Nimesoma au nimesomewa fomu hii ya idhini na nimeweza kujadiliana na mmoja wa wafanyi kazi wa utafiti huu. Maswali yangu yamejibiwa kwa lugha ninayoelewa. Nimeelezwa faida na athari za utafiti huu. Naelewa kuwa kushiriki kwangu ni kwa hiari yangu na ninaweza jiondoa wakati wowote. Nimekubali kushiriki kwenye utafiti kwa hiari yangu mwenyewe.
Ninaelewa kuwa watafiti wataweka juhudi zote kudumisha usiri wangu.
Kwa kupiga sahihi fomu hii, sijawachilia haki zangu za kisheria kama mshiriki kwenye utafiti.

Nimekubali kushiriki kwenye utafiti huu: **Ndio / Hapana**
Nimekubali kupeana ripoti ya histologia: Ndio / Hapana
Nimekubali kupeana nambari yangu ya simu: Ndio / Hapana.

Jina la mshiriki _____

Sahihi ya mshiriki _____

Tarehe _____

TANGAZO LA MTAFITI

Nimempa mshiriki aliyenakiliwa hapa maelezo kuhusu utafiti huu. Naamini kuwa mshiriki ameelewa na amepeana idhini kwa hiari yake mwenyewe.

Jina la mtafiti_____

Sahihi ya mtafiti_____

Tarehe_____

Jukumu kwenye utafiti_____

Jina la shuhuda _____**(***Kama anahitajika.)*

Nambari ya simu_____

Sahihi ya shuhuda_____

Tarehe_____

Appendix IIIa: Minor Assent Form (English)

MINOR ASSENT FORM

Study Title:

PANCREATIC TUMORS: A MULTICENTRE STUDY OF MULTIDETECTOR COMPUTED TOMOGRAPHY FINDINGS AND HISTOPATHOLOGIC CORRELATION IN NAIROBI, KENYA.

Principle Investigator:

Dr. Roseline Kerubo Ogaro, Department of Imaging and Radiation medicine, University of Nairobi.

We are doing a research study about tumours (abnormal growths) of the pancreas in both children and adults within Nairobi. The pancreas is a special organ found at the back of your abdomen. We want to get information on how different tumours of the pancreas look like on CT scan images.

Permission has been obtained to carry out this study by the Kenyatta National Hospital-University of Nairobi Ethics and Research Committee (KNH-UoN ERC) Protocol No. _____.

This research study is a way to learn more about people. At least thirty-nine people will be participating in this research study with you.

If you decide that you want to be part of this study, we will examine the appearance of CT scan images of your abdomen. Your usual doctor may decide that you need a special test called 'biopsy and histology'. This means that a small piece of the disease will be taken from your body to be analysed in the laboratory. Once the results are out, we will need to get that information from your medical records or directly from you or your parents/guardians.

There are some things about this study you should know. We shall do everything to make sure that your information remains confidential. When we finish this study, we will write a report about what was learned. This report will not include your name or that you were in the study.

Your participation will be of benefit to the society. The information obtained will help doctors to better understand tumours of the pancreas and be able to diagnose them faster and more accurately. This will help other children like you in future.

You do not have to be in this study if you do not want to be. If you decide to stop after we begin, that's okay too. This will not change the way you will be treated for your illness in anyway.

Your parents know about the study too.

If you decide you want to be in this study, please sign your name.

I, _____, want to be in this research study.

_____ (Signature/Thumb stamp).

_____(Date).

Researcher's Name: _____

Signature: _____

Date: _____

Role in the study: _____ [i.e. study staff who explained the assent form.]

Appendix IIIb: Minor assent form (Swahili)

FOMU LA IDHINI LA MSHIRIKI MCHANGA

Mada la utafiti:

UVIMBE ZA KONGOSHO: UCHAMBUZI WA MATOKEO YA PICHA YA CT SCAN IKILINGANISHWA NA RIPOTI YA HISTOPATHOLOGIA KATIKA VITUO VITATU MJINI NAIROBI, KENYA.

Mtafiti Mkuu:

Dkt. Roseline Kerubo Ogaro, Idara ya Radiolojia, Chuo Kikuu cha Nairobi.

Tunafanya utafiti kuhusu uvimbe za kongosho miongoni mwa watoto na watu wazima jijini Nairobi. Utafiti huu ni njia moja ya kupata maarifa zaidi juu ya magonjwa ya binadamu, haswa vile uvimbe za kongosho huonekana katika picha ya CT scan. Habari hii tutalinganisha na majibu ya histolojia kutoka kwenye maabara.

Utafiti huu umeruhusiwa na Kamati ya Maadili na Utafiti, hospitali kuu la Kenyatta na Chuo Kikuu cha Nairobi; nambari ya itifaki_____.

Watu wasiopungua thelathini na tisa watashirikishwa kwenye utafiti huu.

Iwapo utaamua kushiriki, tutachunguza mwonekano wa picha zako za CT scan ya tumbo. Daktari wako wa kawaida ataamua kama utafanyiwa kipimo maalum ya histolojia. Hii inamaanisha kuwa kipande kidogo cha uvimbe kitachukuliwa kutoka kwenye mwili wako kisha kifanyiwe uchunguzi kwenye maabara.

Pindi tu majibu yatakapotokea, tutahitaji habari hiyo kutoka rekodi yako ya hospitali ama tutaitisha kutoka kwako au kutoka kwa mzazi / mlezi wako.

Kuna mambo mengine kuhusu utafiti huu unapaswa kufahamu. Tutafanya kila tuwezalo ili kuhakikisha kwamba usiri wako umedumishwa. Maelezo yako binafsi kama jina na nambari ya hospitali yatawekwa siri na hayatakuwepo katika makaratasi ya utafiti na ripoti ya mwisho ya utafiti.

Kushiriki kwako katika utafiti huu utafaidi jamii. Maarifa yatakayopatikana yatawasaidia madaktari kuelewa kwa njia bora zaidi juu ya uvimbe za kongosho. Maarifa haya yatawawezesha madaktari kutambua kwa haraka na usahihi zaidi aina mbali mbali za uvimbe. Hii itawasaidia watoto wengine kama wewe siku za usoni.

Sio lazima ushiriki kwenye utafiti huu kama hutaki. Kuamua kutoshiriki au pia kusitisha kushiriki baada ya kujiunga inakubalika. Hiyo haitasababisha kubadilishwa kwa huduma ya kiafya unayostahili kupata.

Wazazi / walezi wako pia wamejulishwa kuhusu utafiti huu.

Ikiwa umekubali kushirikishwa kwenye utafiti huu andika jina lako kisha uweke sahihi.

Mimi, _____ nimekubali kwa hiari yangu kushiriki kwenye utafiti huu.

_____ Sahihi/ chapisho la kidole.
_____ Tarehe.

Jina la mtafiti_____
Sahihi ya mtafiti_____
Tarehe_____
Jukumu kwenye utafiti_____

Appendix IVa: Parental consent form (English)

Title of Study:

PANCREATIC TUMORS: A MULTICENTRE STUDY OF MULTIDETECTOR COMPUTED TOMOGRAPHY FINDINGS AND HISTOPATHOLOGIC CORRELATION IN NAIROBI, KENYA.

Principal Investigator\and institutional affiliation: Dr. Roseline Kerubo Ogaro, Department of Imaging and Radiation medicine, University of Nairobi.

Introduction:

I would like to tell you about a scientific study being conducted by the above researcher. This consent form will provide you with the information you need to help you decide whether or not your child should participate in the study. Feel free to ask any questions regarding the study for example the possible risks and benefits, the rights of your child as a participant and anything else that may not be clear to you. When satisfied with the information you will have gotten, you may decide if you want your child to be a participant or not. Once you understand and agree to your child being involved in the study, I will request that you write your name on this form and sign against it. You should understand the general principles which apply to all participants in a medical research:

i) Your child's decision to participate is entirely voluntary.
ii) You child may opt to withdraw from the study at any given time without having to give a reason for his/her withdrawal.
iii) Refusal to participate in the research or to withdraw will not have an impact on your child's medical care.

May I continue? YES / NO

For children under 18 years of age we give information about the study to parents or guardians for you to be able to give informed consent for your child's participation. A copy of this form will be given to you for record keeping. If your child is at an age that he/she can understand what is being done then he/she will also be required to agree to participate in the study after receiving information in a language that he/she is able to understand. He/she will then sign an assent form.

WHAT IS THE PURPOSE OF THE STUDY?

The researcher is recruiting individuals who are found to have tumours of the pancreas on computed tomography (CT scan) imaging. The purpose of the study is to expand knowledge about the CT imaging appearances of the different pancreatic tumour types that occur in Kenyan patients. There will be atleast thirty-nine participants in this study.
We are asking for your consent to have your child as one of the participants in the study.

WHAT WILL HAPPEN IF YOU DECIDE YOU WANT YOUR CHILD TO BE IN THIS RESEARCH STUDY?

Even before your child is enrolled into the study, your child's primary doctor will have already requested for him/her to have an abdominal CT scan to further evaluate the illness. The researchers will have access to the findings of your child's CT imaging.

The principal investigator or a research assistant may obtain information from your child's medical records pertaining his/her histopathological report. They may also seek you out to provide the histopathological report if this cannot be obtained from the medical records. Histopathological report refers to the results of any tissue that may be obtained from your child's pancreas for evaluation at the laboratory. These results will be compared to the findings that will be obtained from CT imaging.

We will request that you give us a phone number by which we can contact you if necessary. If you agree to provide your contact information, it will be used only by the study staff and will not be shared with other people. We may need to contact you to provide the histopathological report.

ARE THERE ANY RISKS, HARMS, DISCOMFORTS ASSOCIATED WITH THIS STUDY?

One possible risk of being in this study is loss of confidentiality. All effort will be put in place to minimize the risk. A coded number will be used in the data collection forms to identify your child instead of his/her name and hospital number. A password-protected computer database will be used for electronic information and all paper records will be stored in a locked file cabinet. However, no system of protecting confidentiality can be absolutely fool proof and it

is still possible that someone could find out your child was a participant in this study and could find out information about your child.

ARE THERE ANY BENEFITS OF BEING IN THIS STUDY?

The information obtained from this study will help us better understand the different types of pancreatic tumours that occur in Kenya. It will be a contribution to science and will help to improve promptness and accuracy of diagnosis of pancreatic tumours.

WILL BEING IN THIS STUDY COST YOU ANYTHING?

There will be no additional costs incurred by you more than would have otherwise been incurred. CT imaging of the abdomen and any surgery or biopsy and histology will be recommended by your primary doctor as part of the diagnostic evaluation of your child's illness.

IS THERE REIMBURSEMENT FOR PARTICIPATING IN THIS STUDY?

We do not anticipate that you will use your money to facilitate the study. We will contact and meet you when need arises and we will bear the costs of this. Therefore, there will be no need for a refund.

WHAT IF YOU HAVE QUESTIONS IN FUTURE?

If you have any other queries about your child participating in this study, feel free to contact the study staff using the phone number provided below.

For more information about your child's rights as a research participant, you may also contact the Secretary/Chairperson, Kenyatta National Hospital/University of Nairobi Ethics and Research Committee, Telephone No. 2726300 Ext. 44102, email uonknh_erc@uonbi.ac.ke.

The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

WHAT ARE YOUR OTHER CHOICES?

Your decision to have your child participate in this research is voluntary. You are free to decline or withdraw participation of your child in the study at any time without any explanation and

without any consequences. Just inform the study staff and the participation of your child in the study will be stopped. Withdrawal of your child from the study will not affect the healthcare your child is otherwise entitled to in this health facility or other health facilities.

For more information contact Dr. Roseline Kerubo Ogaro on 0705240278 between 9.00AM and 4.00PM.

CONSENT FORM (STATEMENT OF CONSENT)

Parent/guardian statement

I have read this consent form or had the information read to me. I have discussed this research with a study staff and my questions have been answered in a language that I understand. The risks and benefits associated with the study have been explained to me. I understand that I will be given a copy of this consent form after signing it for my record. I understand that my participation and that of my child in this study is voluntary and I have the choice to withdraw at any time.

I understand that all efforts will be maintain my child's and my confidentiality.

By signing this consent form, I have not given up my child's legal rights as a participant in this research study.

I voluntarily agree to my child's participation in this research study: Yes No

I agree to avail the histopathological report if required: Yes No

I agree to provide contact information for follow-up: Yes No

Parent/Guardian signature /Thumb stamp: _____

Parent/Guardian printed name: _____

Date: _____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the parent/guardian named above and believe that he/she has understood and has voluntarily given his/her consent.

Researcher's Name: _____

Researcher's signature: _____

Date: _____

Role in the study: _____ [i.e. study staff who explained informed consent form.]

Witness Printed Name (If witness is necessary) _____
Signature: _____

Date: _____

Appendix IV(b): Parental consent form(Swahili)

FOMU YA IDHINI KUTOKA KWA MZAZI ILI KUSHIRIKISHA MTOTO KATIKA UTAFITI.

Mada la utafiti:

UVIMBE ZA KONGOSHO: UCHAMBUZI WA MATOKEO YA PICHA YA CT SCAN IKILINGANISHWA NA RIPOTI YA HISTOPATHOLOJIA KATIKA VITUO VITATU MJINI NAIROBI, KENYA.

Mtafiti Mkuu:

Dkt. Roseline Kerubo Ogaro, Idara ya Radiolojia, Chuo Kikuu cha Nairobi.

Utangulizi:

Ningependa kukujulisha juu ya utafiti huu unaohusiana na uvimbe za kongosho ili upate kuwa na habari itakayo kusaidia kuamua kama mwanao anaweza shiriki kwenye utafiti. Una uhuru wa kuuliza swali lolote kuhusiana na utafiti kama vile manufaa au madhara mtoto anaweza pata kutokana na utafiti, haki zake au swali lolote lile. Ukishapata majibu yote ya maswali utakayokuwa nayo, unaweza amua kama mwanao atashiriki kwenye utafiti au la. Ukikubali ashiriki, ningependa uandike jina lako na utie sahihi kwenye fomu hii.

Mambo haya matatu ni muhimu:

1. Kushirikishwa kwa mwanao kwenye utafiti ni kwa hiari yenu.
2. Mwanao anaweza jiondoa kwenye utafiti wakati wowote bila kuhitajika kupeana sababu.
3. Ukiamua mwanao asishirikishwe hakutakuwa na athari zozote na bado atapata matibabu vile anastahili.

Ninaweza endelea? Ndio / Hapana

Kwa watoto walio chini ya miaka kumi na minane, tunawajulisha wazazi kuhusu utafiti huu ili wawe na habari kamili ya kuwawezesha kupeana idhini ya kushirikisha watoto wao. Utapewa nakala ya fomu hii uwe nayo. Kama mtoto wako anaweza elewa kinachoendelea, basi pia yeye atapewa habari hii na atahitajika kupeana idhini kisha ataweka sahihi pia.

Utafiti huu umeidhinishwa na Kamati ya Maadili na Utafiti, hospitali kuu la Kenyatta na Chuo Kikuu cha Nairobi; numbari ya itifaki _____.

Utafiti unahusu nini?

Utafiti huu utashirikisha wagonjwa ambao watapatikana kuwa na uvimbe kwenye kongosho baada ya kufanyiwa picha ya CT scan. Matokeo ya picha yatachambuliwa na kulinganishwa na matokeo ya histolojia. Matokeo ya histolojia hupatikana baada ya sehemu ndogo kwenye uvimbe kutolewa ili ichunguzwe kwenye maabara.

Utafiti huu unanuia kuongeza maarifa zaidi kuhusu aina mbali mbali za uvimbe zinazotokea kwenye kongosho humu nchini Kenya.

Kutakuwa na jumla ya washiriki wasiopungua thelathini na tisa katika utafiti huu. Tungependa upeane idhini ili mwanao aweze kushiriki.

Mambo yapi yatafanyika ukiamua mwanao ashirikishwe kwenye utafiti?

Hata kabla ya kushirikishwa, daktari wa mwanao atakuwa amependekeza afanyiwe CT scan ya tumbo. Watafiti hawa wataweza kupata matokeo hayo na kuona picha zenyewe. Mtafiti mkuu au msaidizi atakagua rekodi za mwanao za matibabu ili apate ripoti ya histolojia. Huenda pia watawasiliana nawe ili kupata ripoti ya histolojia ikiwa habari hiyo haitapatikana kutoka kwa rekodi za matibabu. Ripoti hii italinganishwa na matokeo ya picha ya CT scan.

Tutahitaji utupe nambari yako ya simu ili tuweze kuwasiliana na wewe. Nambari hiyo itatumika na watu wanaofanya utafiti huu pekee na haitapeanwa kwa watu wengine. Tutahitaji kuwasiliana na wewe ili tuweze kupata ripoti ya histolojia.

Kutakuwa na athari zozote kuhusiana na utafiti?

Kuna uwezekano wa kupoteza usiri wa mwanao akishirikishwa kwenye utafiti huu. Tutaweka juhudi zote ziwezekanazo ili isifanyike hivyo. Taarifa yote kutoka kwenu, kutoka kwa rekodi za matibabu na matokeo ya picha itawekwa siri. Jina la mwanao, nambari yake ya hospitali na taarifa yoyote ya kumtambulisha haitawekwa kwenye ripoti ya utafiti huu. Nambari maalum ndio itakayotumika badala ya jina lake na nambari yake ya hospitali. Kompyuta itakayotumika itakuwa na nywila ili kuzuia watu wasiokuwa na idhini kupata habari yake. Makaratasi yote yatakayotumika yatawekwa kwenye kabati linalofungwa na kifunguu. Walakini, hata tukichukua hatua zote ziwezekanavyo, kuna uwezekano kuwa mtu asiye na idhini bado anaweza pata taarifa ya afya ya mwanao.

Kutakuwa na faida yoyote katika kushiriki kwenye utafiti?

Kushiriki itakuwa ni changio kwa ufahamu wa sayansi. Maarifa yatakayotokana na utafiti huu yataboresha utambuzi wa aina mbali mbali za uvimbe za kongosho kwa haraka na usahihi miongoni mwa madaktari nchini Kenya.

Kushiriki itakugharimu chochote?

Utafiti huu hautakugharimu pesa ziada kwani picha ya CT scan na uchunguzi wa histolojia zitakuwa zimependekezwa na daktari wako wa kibinafsi ili aweze kutambua ugonjwa wa mwanao.

Utarudishiwa pesa yoyote utakayotumia kwenye utafiti?

Kwa sababu hakuna pesa zaidi utagharimika, hakuna pesa utakayorudishiwa. Tutakapohitajika kuwasiliana au kukutana nawe, sisi wenyewe tutafanya hivyo na gharama itakuwa kwetu sisi.

Na je ukiwa na maswali yoyote siku za usoni?

Ukiwa na swali lolote kuhusu utafiti huu, unaweza kuwasiliana na Dkt. Roseline Kerubo Ogaro kupitia namba ya rununu 0705240278 kutoka saa tatu asubuhi, hadi saa kumi alasiri.

Ukihitaji habari zaidi kuhusu haki ya mwanao kama mshiriki kwenye utafiti unaweza pia kuwasiliana na karani / mwenyekiti, Kamati ya Maadili na Utafiti ya hospitali kuu ya Kenyatta / Chuo Kikuu cha Nairobi kupitia nambari ya simu: (020) 2726300 Ext 44102, barua pepe: uonknh_erc@uonbi.ac.ke.

Wafanyikazi wa utafiti watakurudishia pesa utakayotumia kupiga simu ikiwa unapiga kuhusiana utafiti huu.

Una chaguo lingine?

Uchaguzi wa kushirikisha mwanao kwenye utafiti ni kwa hiari yako. Una uhuru kutokubali ashirikishwe na unaweza pia amua kumwondoa kwenye utafiti wakati wowote. Ukitueleza umeamua kumuondoa basi tutafanya hivyo. Kumuondoa hakutasababisha matokeo yoyote kwenye matibabu ya mwanao.

FOMU YA IDHINI

TANGAZO LA MZAZI/MLEZI.

Nimesoma au nimesomewa fomu hii ya idhini na nimeweza kujadiliana na mmoja wa wafanyi kazi wa utafiti huu. Maswali yangu yamejibiwa kwa lugha ninayoelewa. Nimeelezwa faida na athari za utafiti huu. Naelewa kuwa kushirikikisha mtoto wangu ni kwa hiari yangu na ninaweza muondoa wakati wowote. Nimekubali kumshirikisha kwenye utafiti kwa hiari yangu mwenyewe.

Ninaelewa kuwa watafiti wataweka juhudi zote kudumisha usiri wa mwanangu.

Kwa kupiga sahihi fomu hii, sijawachilia haki za mtoto wangu za kisheria kama mshiriki kwenye utafiti.

Nimekubali mtoto wangu ashiriki kwenye utafiti huu: Ndio /Hapana

Nimekubali kupeana ripoti ya histolojia: Ndio / hapana

Nimekubali kupeana nambari yangu ya simu: Ndio / Hapana.

Jina la mshiriki _____

Sahihi ya mshiriki _____

Tarehe _____

TANGAZO LA MTAFITI

Nimempa mzazi/ mlezi aliyenakiliwa hapa maelezo kuhusu utafiti huu. Naamini kuwa ameelewa na amepeana idhini kwa hiari yake ili mwanawe ashirikishwe kwenye utafiti huu.

Jina la mtafiti _____

Sahihi ya mtafiti _____

Tarehe _____

Jukumu kwenye utafiti_____

Jina la shuhuda _____(*Kama anahitajika.)*

Nambari ya simu_____

Sahihi ya shuhuda_____Tarehe_____

_____

Appendix V: Data Collection Tool

PANCREATIC TUMORS: A MULTICENTRE STUDY OF MULTIDETECTOR COMPUTED TOMOGRAPHY FINDINGS AND HISTOPATHOLOGIC CORRELATION IN NAIROBI, KENYA.

Section 1: Demographic data

Age / Year of birth	
Sex	o Male o Female

Section 2: MDCT imaging characteristics

Known extrapancreatic malignancy	o Yes o No	o Specify site……
Tumour multiplicity	o Solitary o Multifocal o Diffuse infiltration	
Pancreatic location of tumour	o Head o Uncinate process o Neck o Body o Tail	
Size of tumour (longest dimension in any plane in cm)	o ……	
Tumour margins	o Well circumscribed o Partially circumscribed o Poorly circumscribed	
Homogeneity	o Homogenous o Heterogenous	

Shape	o Smooth o Lobulated o Irregular
Presence of a capsule	o Present o Absent
Internal architecture	o Solid o Cystic o Mixed solid and cystic
Septations	o Unilocular o Multilocular
Cyst communication with pancreatic duct	o Present o Absent
Size of largest cyst (longest dimension in any plane in cm)	o …… o <2cm(microcystic) o ≥2cm(macrocystic)
Attenuation characteristics	
Pre-contrast	o Hypoattenuating o Hyperattenuating o Isoattenuating
Pancreatic phase	o Homogenous o Heterogenous o Rim enhancement o Hypovascular o Hypervascular
Porto-venous phase	o Homogenous o Heterogenous o Rim enhancement o Hypovascular o Hypervascular
Calcification	o Present o Central

- Peripheral

	o Absent
Localised bulge in pancreatic contour	o Present
	o Absent
Abrupt pancreatic duct cut off	o Present
	o Absent
Abrupt biliary duct cut off	o Present
	o Absent
Main pancreatic duct dilatation	o Present
	o Absent
Common bile duct dilatation	o Present
	o Absent
Double duct sign	o Present
	o Absent
Distal pancreatic atrophy	o Present
	o Absent
Mural nodule within a pancreatic duct	o Present
	o Absent
Cyst communication with pancreatic duct	o Present
	o Absent
Local invasion	
Stomach	o Present
	o Absent
Duodenum	o Present
	o Absent
Spleen	o Present
	o Absent
Bile duct	o Present
	o Absent
Kidneys	o Present

- Absent

Other
- ……

Vascular involvement

Hepatic artery
- Abutment
- Encasement
- Calibre change
- Thrombosis

Celiac trunk
- Abutment
- Encasement
- Calibre change
- Thrombosis

SMA
- Abutment
- Encasement
- Calibre change
- Thrombosis

SMV
- Abutment
- Encasement
- Calibre change
- Thrombosis

Splenic vein
- Abutment
- Encasement
- Calibre change
- Thrombosis

Portal vein
- Abutment
- Encasement
- Calibre change
- Thrombosis

IVC/SV/Aorta

Regional nodal involvement
- Present
- Absent

Distant metastasis
- Present

- Absent

Section 3: Prevalence of different pancreatic tumours and MDCT diagnostic accuracy

Likely tumour type from MDCT imaging findings	o Pancreatic ductal carcinoma o IPMN o MD-IPMN o BD-IPMN o SCN o MCN o Pancreatic lymphoma o Pancreatic neuroendocrine tumour o SPN o Secondary tumours o Other……..…….
Histological diagnosis	o Pancreatic ductal carcinoma o IPMN o MD-IPMN o BD-IPMN o SCN o MCN o Pancreatic lymphoma o Pancreatic neuroendocrine tumour o SPN o Secondary tumours o Other…….

Appendix VI. ERC Approval Letter

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KENYATTA NATIONAL HOSPITAL - APPROVED - 16 JUL 2020 - KNH/UoN-ERC - P.O. BOX 20723 - 00202 NAIROBI

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/229

16th July 2020

Dr. Roseline Kerubo Ogaro
Reg. NO.H58/6849/17
Dept.of Diagnostic Imaging and Radiation Medicine
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr Ogaro

RESEARCH PROPOSAL – PANCREATIC TUMORS: A MULTICENTRE STUDY OF MULTIDETECTOR COMPUTER TOMOGRAPHY FINDINGS AND ITS PATHOLOGIC CORRELATION IN NAIROBI, KENYA (P67/02/2020)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 16th July 2020 – 15th July 2021.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

Protect to discover

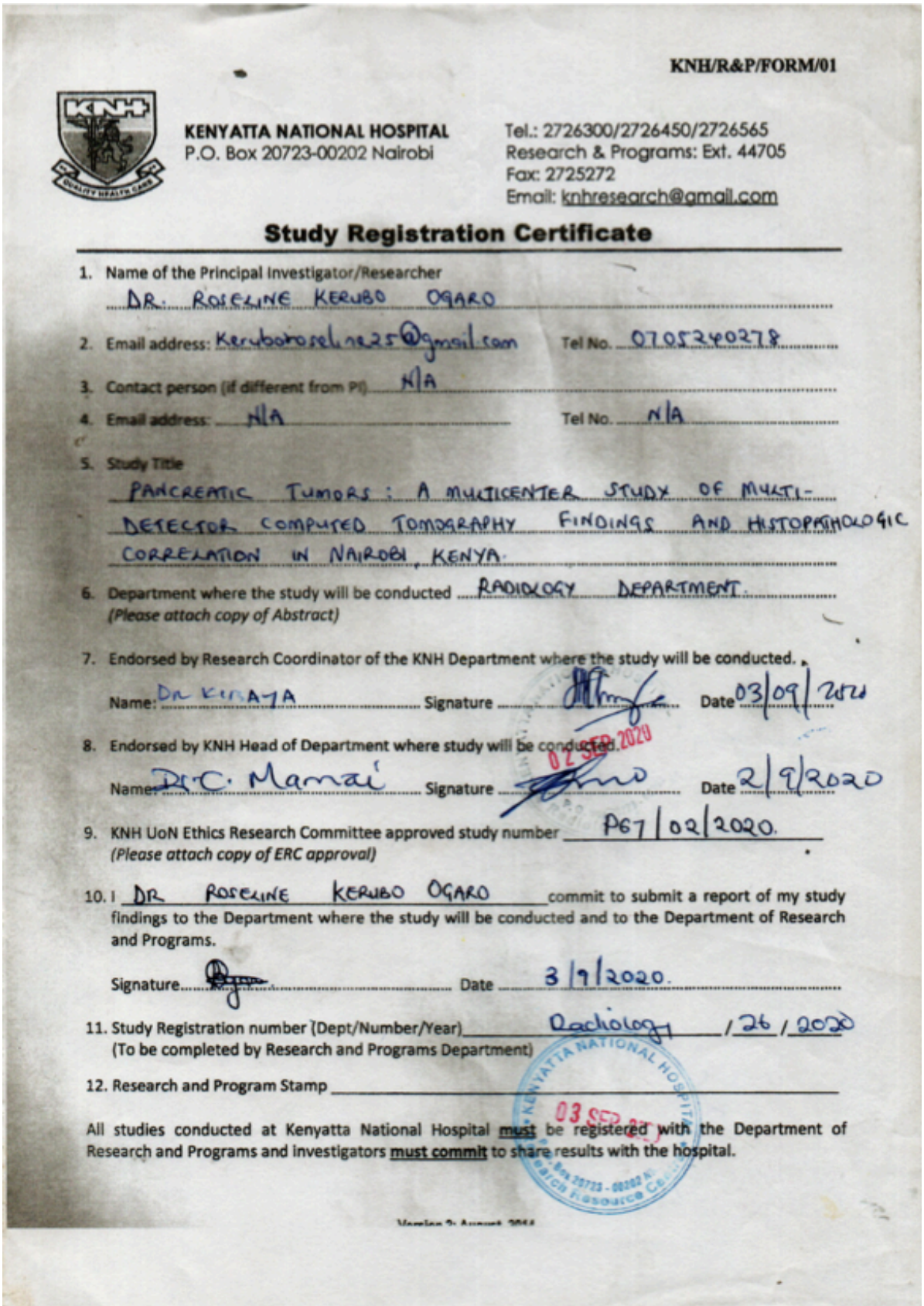
For more details consult the KNH- UoN ERC website http://www.erc.uonbi.ac.ke

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Dean, School of Medicine, UoN
The Chair, Dept.of Diagnostic Imaging and Radiation Medicine, UoN
Supervisors: Dr. Timothy Musila Mutala,Dept.of Diagnostic Imaging and Rad. Medicine,UoN
Dr. Alfred Odhiambo, Dept.of Diagnostic Imaging and Rad. Medicine,UoN
Dr. Wairimu Waweru, Dept.of Human Pathology, UON

Appendix VII. Kenyatta National Hospital Approval Letter



KNH/R&P/FORM/01

KENYATTA NATIONAL HOSPITAL
P.O. Box 20723-00202 Nairobi

Tel.: 2726300/2726450/2726565
Research & Programs: Ext. 44705
Fax: 2725272
Email: knhresearch@gmail.com

Study Registration Certificate

1. Name of the Principal Investigator/Researcher
   DR. ROSELINE KERUBO OGARO
2. Email address: Kerubo roseline25@gmail.com Tel No. 0705240278
3. Contact person (if different from PI) N/A
4. Email address: N/A Tel No. N/A
5. Study Title
   PANCREATIC TUMORS : A MULTICENTER STUDY OF MULTI-DETECTOR COMPUTED TOMOGRAPHY FINDINGS AND HISTOPATHOLOGIC CORRELATION IN NAIROBI, KENYA.
6. Department where the study will be conducted RADIOLOGY DEPARTMENT.
   (Please attach copy of Abstract)
7. Endorsed by Research Coordinator of the KNH Department where the study will be conducted.
   Name: DR KINAYA Signature ..... Date 03/09/2020
8. Endorsed by KNH Head of Department where study will be conducted.
   Name: Dr C. Mamai Signature ..... Date 2/9/2020
   02 SEP 2020
9. KNH UoN Ethics Research Committee approved study number P67/02/2020.
   (Please attach copy of ERC approval)
10. I DR ROSELINE KERUBO OGARO commit to submit a report of my study findings to the Department where the study will be conducted and to the Department of Research and Programs.
    Signature ..... Date 3/9/2020.
11. Study Registration number (Dept/Number/Year) Radiology /26/2020
    (To be completed by Research and Programs Department)
12. Research and Program Stamp
    KENYATTA NATIONAL HOSPITAL
    03 SEP 20
    Research Resource Centre

All studies conducted at Kenyatta National Hospital must be registered with the Department of Research and Programs and investigators must commit to share results with the hospital.