Preoperative Local Staging of Rectal Cancer with Magnetic Resonance Imaging with Pathologic Correlation in Kenyan Patients.

Fiona Achieng' Anyumba

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A research proposal submitted in the University of Nairobi Department of Diagnostic Imaging and Radiation Medicine in partial fulfillment of the requirement for the award of Master of Medicine degree in Diagnostic Radiology at the University of Nairobi

DECLARATION

This is my original work, and to the best of my knowledge, it has not been presented anywhere else in medical literature.

Investigator:

Signature..... Date 15/11/21

Fiona Achieng' Anyumba

This research proposal has been submitted for examination with our approval as University Supervisors:

1. **Dr. Alfred Odhiambo; MBChB, M.Med (Diagnostic Radiology), Fellow (Neuroradiology)**
   Senior lecturer,
   Department of Diagnostic Imaging and Radiation Medicine,
   School of Medicine, University of Nairobi

   Signature..... Date 8/11/2021

2. **Dr. Timothy Musila Mutala; MBChB, M.Med (Diagnostic Radiology)**
   Lecturer,
   Department of Diagnostic Imaging and Radiation Medicine,
   School of Medicine, University of Nairobi

   Signature... ..... Date 8/11/21

3. **Dr. Wairimu Waweru; MBChB, M.Med (Pathology), FCPathECSA**
   Senior lecturer,
   Department of Pathology,
   School of Medicine, University of Nairobi

   Signature..... Date 2/11/2021

4. **Dr. Jane Mugure: MBChB, M.Med (General Surgery)**
   Lecturer,
   Department of Surgery,
   School of Medicine, University of Nairobi

   Signature..... Date 8/11/21

LIST OF ACRONYMS

AJCC- American Joint Committee on Cancer

ANOVA- Analysis of Variance

CEA- Carcinoembryonic Antigen

CI- Confidence Interval

CRM- Circumferential Resection Margin

CT- Computed Tomography

DWI- Diffusion Weighted Imaging

EMVI- Extramural Vascular Invasion

FSE- Fast Spin Echo

KNH- Kenyatta National Hospital

MOH- Ministry of Health

MRI- Magnetic Resonance Imaging

MRF- Mesorectal Fascia

NPV- Negative Predictive Value

PET/CT- Positron Emission Tomography Computed Tomography

PPV- Positive Predictive value

RC- Rectal Carcinoma

SPSS- Statistical Package for Social Sciences

SSS- Sphincter Sparing Surgery

T- Tesla

T2WI- T2 Weighted Imaging

TME- Total Mesorectal Excision

TNM- Tumor-Node-Metastasis

UON- University of Nairobi

TABLE OF CONTENTS

ABSTRACT

Background

Rectal cancer (RC) is a leading cause of cancer related morbidity and mortality in the Kenyan population. Its incidence has increased from 12.3 to 12.9 per 100,000 people per year. Magnetic Resonance Imaging (MRI) is currently the most accurate imaging modality in the loco-regional staging of RC because of its superior soft tissue contrast and multiplanar capability and is used in planning surgical approach, assessing need for additional therapy pre and post- operatively and predicting overall prognosis. This study seeks to evaluate the diagnostic accuracy of MRI in loco-regional staging of RC.

Broad objective

To establish whether preoperative local MRI staging performed using recommended protocols corresponds with the pathological tumor (T) and nodal (N) stage in patients with rectal carcinoma between October 2020 and January 2021.

Methodology

A prospective, cross-sectional study was carried out among patients with RC presenting for MRI at Kenyatta National Hospital and Plaza Imaging Centre. MRI studies of 48 patients were reviewed and T and N stage, MRF and CRM involvement were assigned. Histopathologic assessment was then done postoperatively. The findings were keyed in Microsoft Excel and imported to IBM SPSS Statistics version 21 for analysis and 2x2 tables were constructed to determine the diagnostic accuracy of MRI as a preoperative loco-regional staging tool.

Results

The sensitivity, specificity, PPV, NPV and accuracy of MRI in the T staging of rectal tumors were 85.7%, 92.8%, 97.2%, 66.7% and 91.8%. The MRI sensitivity, specificity, NPV, PPV and accuracy in assessment of MRF involvement were 85.5%, 94.4%, 85.5%, 94.4% and 92%. As regards CRM evaluation, the sensitivity, specificity, PPV and NPV and accuracy were 83.3%, 92.3%, 90.9%, 85.7% and 88% respectively. The nodal sensitivity, specificity, PPV, NPV and accuracy were 85.7%, 92.8%, 97.2%, 66.7% and 91.8%

Conclusion.

MRI has high diagnostic accuracy in evaluation of depth of tumor spread, MRF and CRM assessment and evaluation of metastatic nodal involvement. It should therefore be used as the primary tool in the local staging of RC.

CHAPTER 1: INTRODUCTION

1.1 Background information

Globally the number of new cancer cases and its associated mortality is on the rise, increasing from 14.1 million cases in 2012 to 18.1 million cases in 2018. The World Health Organization projects an increase in incidence to 22 million cases per year in the next 20 years (1). Currently, the 8th most common malignancy worldwide is rectal cancer, making up 3.9% of all cancers and 3.2% of all cancer deaths. In 2018, 1.8 million new cases and 881,000 resultant deaths were estimated to have occurred (2). RC is the 13th most common cancer in Kenya, making up 3% of all the malignancies (2). Though data is inconsistent, available studies show an increase in incidence rates from 12.3 to 12.9 per 100,000 people per year. Compared to western countries, it is seen in younger patients (3).

The surge in the number of cancer cases is largely attributed to changes in lifestyle, which have resulted in differences in diet and physical activity. Increased intake of alcohol, red and processed meats, and micronutrient deficiency particularly folate and calcium which are associated with westernization of our way of life have been found to predispose to the development of colorectal cancer (4). Other risk factors not related to diet include having a first degree relative with colon or rectal cancer, smoking history, obesity, and hormone replacement therapy in postmenopausal women (5). Improvements in imaging modalities particularly cross sectional methods have also increased its detection (6).

Staging of rectal tumors is essential for treatment planning, predicting tumor recurrence and prognosis. The most universally accepted staging system for RC is the tumor-node-metastasis (TNM) system which takes into consideration the tumor size and depth of invasion, the size and number of nodes involved and the presence or absence of metastases (7).

Numerous investigations are performed to conclusively determine the extent of tumor. Physical examination gives a rough idea of the location of tumor and its fixation to adjacent structures as well as sphincter involvement (8). Rectosigmoidoscopy is done to visualize tumor and assess its dimensions, distance from the anal sphincter and relation to surrounding tissues, all of which have an impact on management decisions. Tissue can also be obtained for histologic diagnosis (7). Tumor markers particularly carcinoembryonic antigen (CEA) are

of limited use in initial diagnosis of rectal cancer though high levels preoperatively portend a worse prognosis (9). Radiological studies are indispensable in defining local characteristics of the tumor and checking for distant metastases (7)(8).

Multiple imaging modalities are used in the characterization of rectal tumors, each with its merits and limitations. Due to its superior soft tissue contrast, MRI is the gold standard of imaging of the rectum, with an accuracy of 55-86% in T staging and 39-95% in N staging (10). Technologic advances have improved its ability to depict the layers of the wall of the rectum as well as its surrounding anatomy including the mesorectal fascia and fat. These are key structures in staging local disease and cannot be visualized by other imaging techniques making MRI the modality of choice. It is also able to show sphincter involvement and involvement of the levator ani in low rectal cancers (11). Imaging using the right protocols is the cornerstone of accurate MRI staging (12).

Endoscopic ultrasound is useful for T1 and T2 tumors confined to the rectal wall, and has an accuracy of 67-93% in T staging and 60% in N staging (13). It allows for direct visualization of the tumor and can be used to guide biopsy. However, it is operator dependent, often over stages tumors that invade the muscularis propria and is inappropriate in staging advanced T3 or T4 tumors because the mesorectal fascia is not visualized by ultrasound. Its use is also limited in staging of upper rectal tumors and those that cause stenosis of the bowel wall (14).

Computed tomography (CT) is often used in the initial diagnostic workup of RC but has been found to be suboptimal in assessment of tumor size and extension as well as nodal status in rectal tumors due to its inferior soft tissue contrast with an accuracy of 33-77% in T staging and 22-73% in N staging. Its utility is mainly in detecting metastases (13). In contrast, it is the cornerstone in imaging colonic tumors, with a sensitivity of 90% and a specificity of 69%. Its role is more limited in N staging, the sensitivity and specificity being 71% and 67% respectively (15).

Positron emission tomography-computed tomography (PET /CT) is useful in nodal staging of RC as well as metastatic screening and is of benefit in radiation therapy planning, assessing response to therapy and detection of residual or recurrent disease after initial treatment (16).

Recently, the Ministry of Health (MOH) recommended MRI as the imaging tool of choice for local staging of RC (17). This study aims to assess the sensitivity and specificity of MRI in RC staging by comparing imaging findings with postoperative histopathologic diagnosis. This would give us local data to support the implementation of the MOH guidelines and also aid in the development of best practice protocols to be applied to RC imaging in the country.

CHAPTER 2: LITERATURE REVIEW

2.1. Introduction

Rectal cancer is one of the most frequently diagnosed malignancies of the gastrointestinal tract (2). Its management has changed over time; in the past the patient was mainly managed by the surgeon but now many centers form multidisciplinary teams (MDTs) which incorporate other specialists including oncologists, pathologists, radiologists, gastroenterologists and radiation oncologists in the treatment planning of RC patients. This has been shown to improve long term survival (18). Improvements in imaging modalities, oncologic developments and an increase in surgical alternatives have resulted in better outcomes (19). In Netherlands, the five year survival rate of RC has improved from 51% in 1989 to 65% in 2014 (20). However, mortality and recurrence rates in Kenya are still high (3)(21).

Radiology is key in the staging and follow up of RC. It is useful in preoperative staging, planning of surgical approach, evaluation of treatment response and assessment of recurrent disease (22)(23). High resolution MRI is the superior modality of choice due to its more advanced soft tissue contrast, multiplanar ability and capability to perform functional imaging (10). It is the modality that most accurately depicts the rectal wall layers and demonstrates the surrounding mesorectal fat, MRF and pelvic floor as well as invasion of tumor into surrounding tissues. It also gives information on nodal status (11). It has an overall sensitivity of and specificity of 87% and 75% in T staging and 77% and 71% in N staging, making it superior to other imaging techniques in the delineation of rectal masses (24).

2.2. Anorectal anatomy

The most distal part of the large intestine is the rectum and it extends from rectosigmoid junction to the anal canal. It is about 15 centimeters long and is divided into three parts. The lower third extends 0 to 5 centimeters from the anal verge, the middle third 6 to 10 centimeters and the upper third 11 to 15 centimeters. The proximal rectum is intraperitoneal, the rest extraperitoneal (25).

A layer of fat encircles the rectum forming the mesorectum. It contains blood vessels, lymph nodes and fibrous septa. This perirectal fat is bound laterally by connective tissue known as the mesorectal fascia (MRF). It is thinner anteriorly and thicker posterolaterally and disappears about 2 cm above the puborectalis muscle (Figure 1) (26).

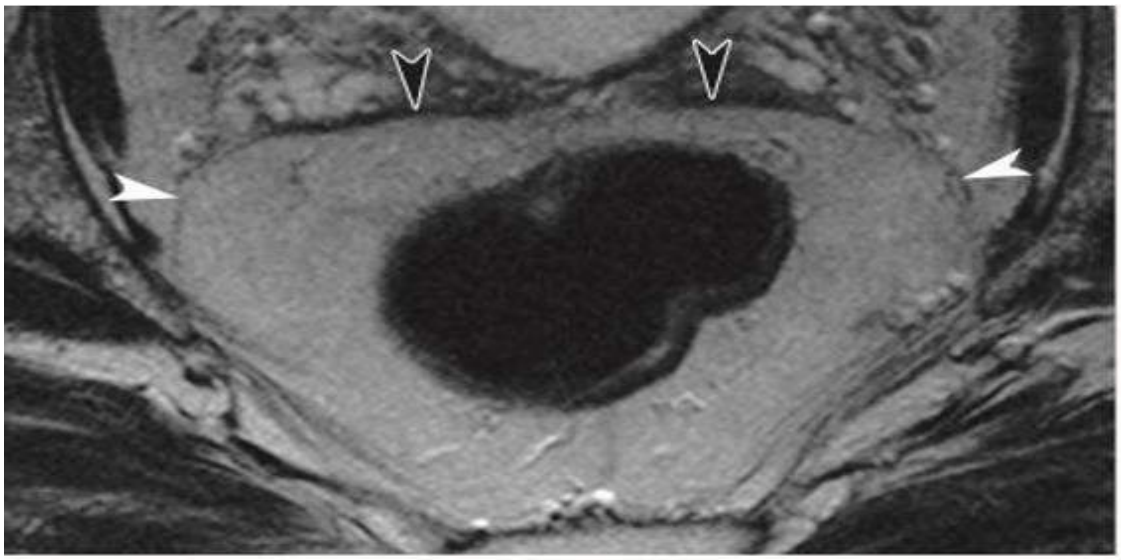


Fig 1- Normal mesorectal anatomy. Axial T2 weighted MR image depicts the mesorectal fascia as a thin, hypointense band (white arrowheads) surrounding hyperintense mesorectal fat. Anteriorly, the fascia appears more thickened and is difficult to differentiate from the Denonviller fascia (black arrowheads)

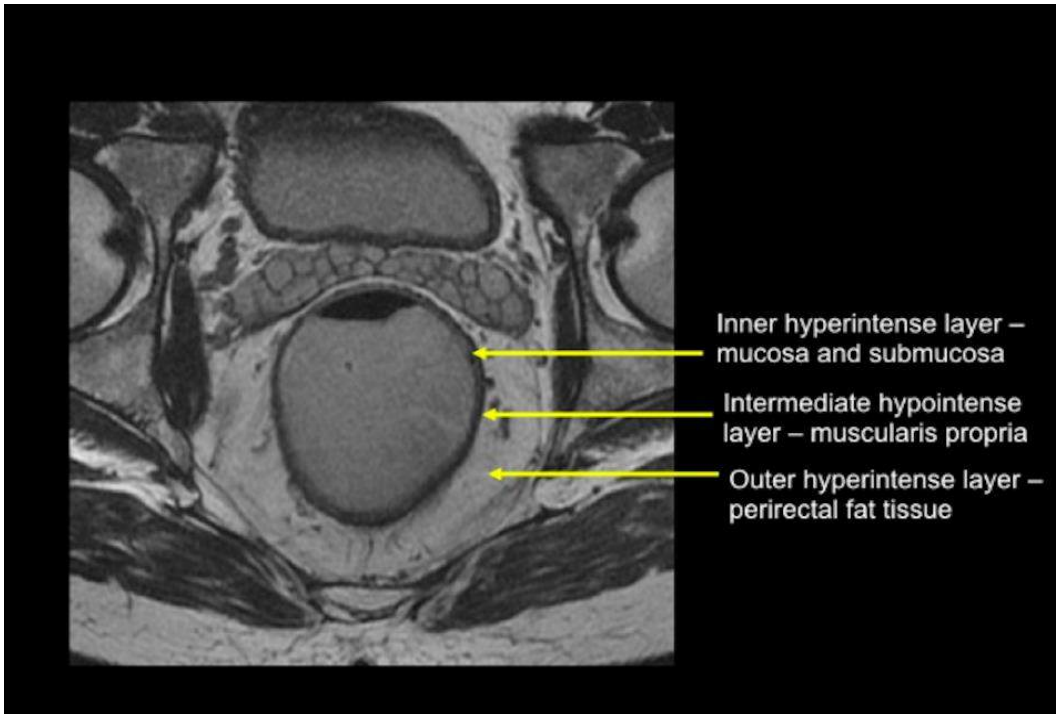


Fig 2- Rectal wall layers. Axial T2 weighted MR shows an inner hyperintense layer representing the mucosa and submucosa and intermediate hypointense layer representing the muscularis propria. The rectum is surrounded by hyperintense perirectal fat

High resolution MRI is able to delineate the rectal wall layers. On T2 weighted imaging (T2WI), the mucosa and submucosa are hyperintense, the muscularis propria is hypointense and the perirectal fat seen as an outer hyperintense layer. The MRF is seen as a narrow hypointense layer around the mesorectum (Figure 2)(27).

The anus extends from the anorectal junction, represented on imaging as the point at which the levator ani muscle inserts into the rectum, to the anal verge. It is about 4 centimeters long in adults and is longer in males. (23). It is cylindrical in shape and has two layers. The innermost layer is formed by the internal anal sphincter and the outermost by the external anal sphincter. The external sphincter is T2 hypointense and the internal sphincter relatively hyperintense (Figure 3). The levator ani complex forms a sling supporting the pelvic structures and is composed of the puborectalis, pubococcygeus, ileococcygeous, and coccygeous muscles. The complex is easily identified on coronal T2WI as a hypointense funnel shaped diaphragm forming the pelvic floor (26).

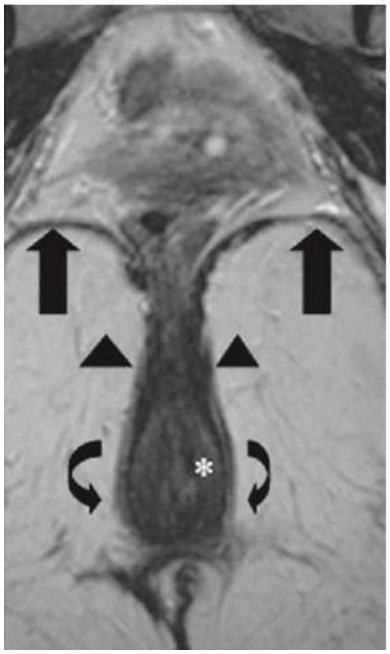


Figure 3- Normal anal sphincter complex. Coronal T2 weighted MR image shows the levator ani muscle as a hypointense structure (black arrows) forming the pelvic floor. The puborectalis muscle (arrowheads) is depicted at the insertion of the levator ani muscle onto the anal canal. The external (curved arrows) and internal (asterisk) anal sphincters are also seen.

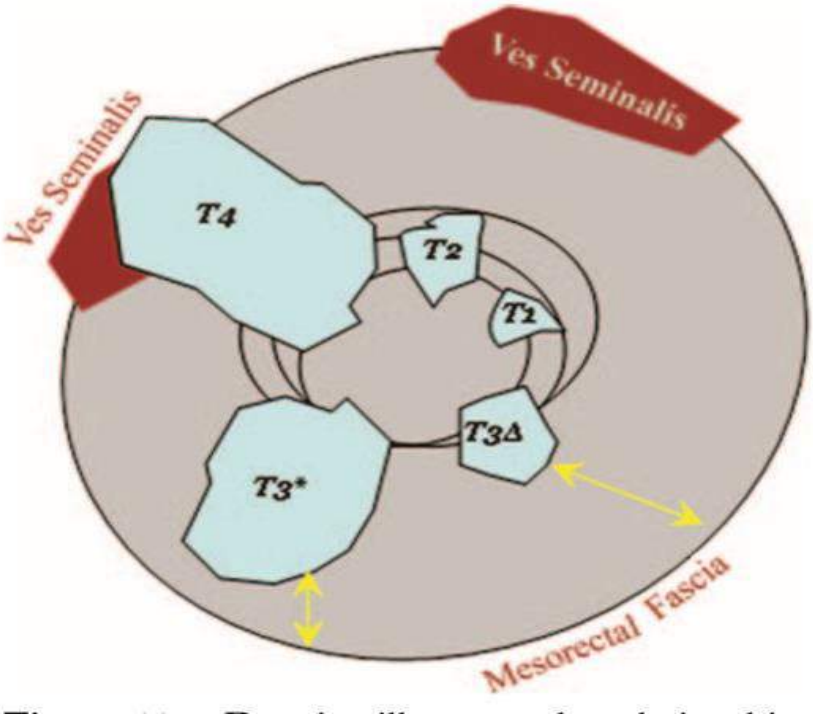


Fig 4-Drawing illustrating the relationship between CRM and rectal tumors of various stages. The most important predictor of local recurrence is a short tumor- mesorectal distance (double headed arrows) with a CRM of less than 1mm associated with a higher rate of recurrence.. Therefore T3 tumors with a narrow CRM (T3*) are more likely to recur.

Decisions on the surgical technique to be used as well as its extent are dependent on the preoperative stage of disease as depicted by MRI. Total Mesorectal Excision (TME) is the surgical procedure of choice for rectal tumors. A study done in Switzerland compared TME to conventional surgery and found that it had lower recurrence rates (20.8% versus 5.9%) and improved overall survival (28). The MRF represents the circumferential resection margin (CRM) in TME, which is defined as the interval between the margin of the tumor to the edge of the resected specimen (29). A CRM of less than 1 millimeter is associated with higher recurrence rates (Figure 4) (30). Accurate identification of the distance between the tumor and the MRF on high resolution MRI is therefore paramount in treatment planning. If the CRM is less than 1 millimeter the patient will require neoadjuvant chemoradiotherapy prior to surgery and this has been shown to reduce reoccurrence of the tumor to 6% (31). However, utility of CRM is limited in tumors located anteriorly and in slimmer patients with minimal perirectal fat (27). The surgical planes are shown in Figure 5.

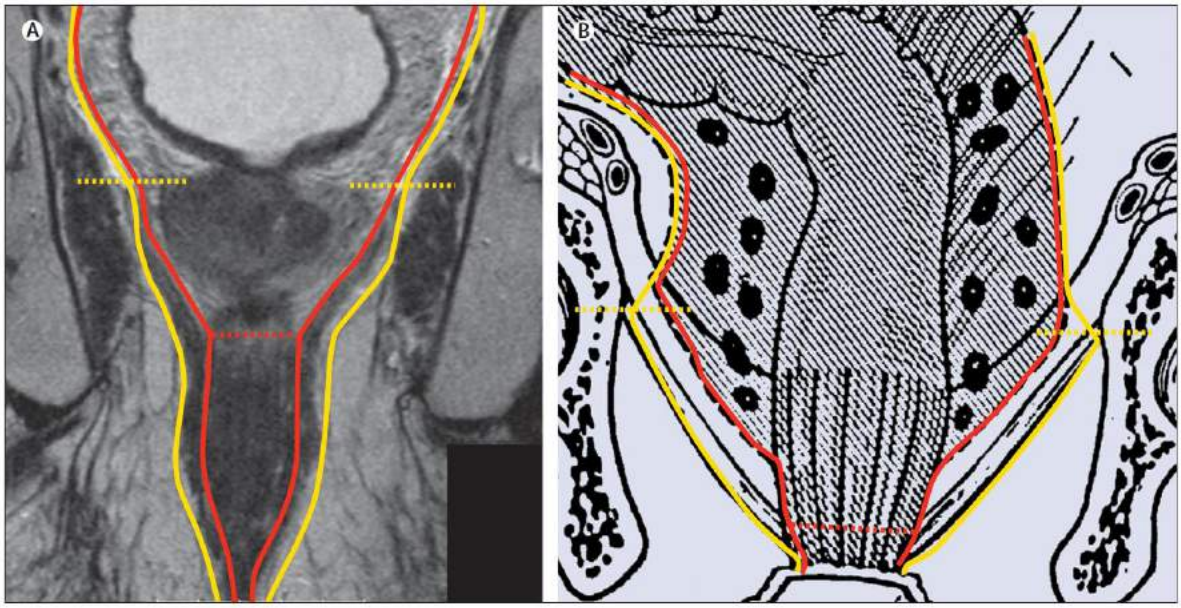


Fig 5: Planes of resection in RC surgery. The mesorectal plane is shown in red and the extralevator plane in yellow. Perineal and abdominal portions meet at the dashed yellow lines.

MRI also has the ability to precisely assess the anal sphincters and determine the distance from the tumor margin to the anal verge and can therefore give guidance to surgeons in regard to sphincter sparing surgery (SSS) in middle and lower RC (32). According to a study done in Egypt, SSS leads to a better quality of life by eliminating the need for a permanent colostomy and also has oncologic outcomes comparable to abdominoperineal resection in patients with disease free sphincters (33).

2.3. MRI technique in rectal cancer imaging

Magnetic field strength of 1.5T is suitable to depict rectal anatomy (22)(23). Imaging at 3T should theoretically result in better quality images by doubling the signal to noise ratio (34) and thereby clearly delineate bowel wall invasion but this has not been demonstrated in practice (35).

Either external pelvic phased- array coils or endorectal coils may be used. Endorectal coils clearly show the layers of the bowel wall thus enhancing the accuracy of T-staging comparable to that of endorectal ultrasound but it is not comfortable to the patient. In addition it is of limited application in high rectal tumors and tumors that cause stenosis of the lumen. Moreover, the perirectal structures are not included in its field of view. Its use is currently not recommended. Phased array coils provide high resolution images, clearly depicting the mesorectum and MRF but may not distinguish between T1 and T2 and also T2 from equivocal T3 tumors (36)

Patients should be well prepared to optimize imaging. They should be informed about the time it will take to perform the study. Enemas, bowel contrast or luminal distention is not necessary. The patient should have an empty bladder. Analgesia and sedation may be administered if necessary and should be prepared beforehand. Antispasmodics are not required but may enhance image quality. Use of intravenous contrast may overstage the tumor by causing enhancement of vessels therefore obscuring fat planes of the pelvis (23)The patient should then be placed supine within the MRI table and the surface coil placed to cover from the level of the bifurcation of the aorta to the anal verge (37).

Use of correct protocols is the cornerstone of accurate imaging. A study done by Suzuki et al showed that among patients with a higher inaccuracy of staging, the number of sequences was higher and imaging was more commonly performed with contrast enhancement (12).

Two dimensional fast spin echo (FSE) T2 weighted sequences without fat suppression with a small field of view and a 3-5 millimeter slice thickness and 1 millimeter gap are recommended by the MERCURY group. Planes of acquisition include oblique axial, sagittal (which is dependent on the longitudinal axis of the tumor) and oblique coronal (to delineate low rectal tumors and the sphincters). The plane of imaging must be perpendicular to the MRF to enable assessment of its invasion by tumor and adequately describe the CRM (38). Inaccurate obliquity of the axial plane will make the muscularis propria indistinct and lead to erroneous T staging. FSE T2 weighted images with a large field of view are then acquired to evaluate lymph nodes outside the mesorectum as well as extramural vascular invasion.

In addition, the Society of Abdominal Radiology (SAR) rectal cancer disease-focused panel (DFP) recommend an unenhanced T1 weighted sequence and for lower rectal tumors a coronal T2 sequence obtained parallel to the anal canal to check for sphincter involvement. It however discourages acquisition of contrast enhanced and dynamic contrast enhanced T1 weighted, three dimensional T2 weighted and fat saturated sequences. Diffusion weighted imaging (DWI) sequences are necessary for restaging (39)(40).

2.4. Staging and management principles of rectal cancer.

Staging of RC gives information on extent of spread of the malignancy which is essential in selecting treatment options and predicting prognosis and response to therapy. It determines the degree of excision, need for neoadjuvant therapy, any treatment required after surgical treatment and the overall goal of management (27)(40).

Formulated by the American Joint Committee of Cancer (AJCC), the TNM system is currently the most widely used in staging of RC (37). The T stage gives information on the depth of tumor spread, the N on nodal involvement and the M on metastatic spread (7). Tumors involving the mucosa and submucosa are designated T1, those invading the muscularis propria T2, T3 tumors invade the perirectal fat and T4 invade adjacent structures including the bladder, prostate and pelvic side wall (Figure 5). T3 tumors are further divided into 4 categories based on height of tumor from muscularis propria; T3a less than 1millimeter, T3b 1-5millimeters, T3c 5-15mm and T3d more than 15mm. While T1 and T2 tumors are treated by surgical resection, T3 and T4 require preoperative chemoradiation. Therefore distinction between T2 and T3 tumors which can be done by MRI is essential in determining management (41). Overall accuracy of T staging is above 90% in most studies (23)(10).

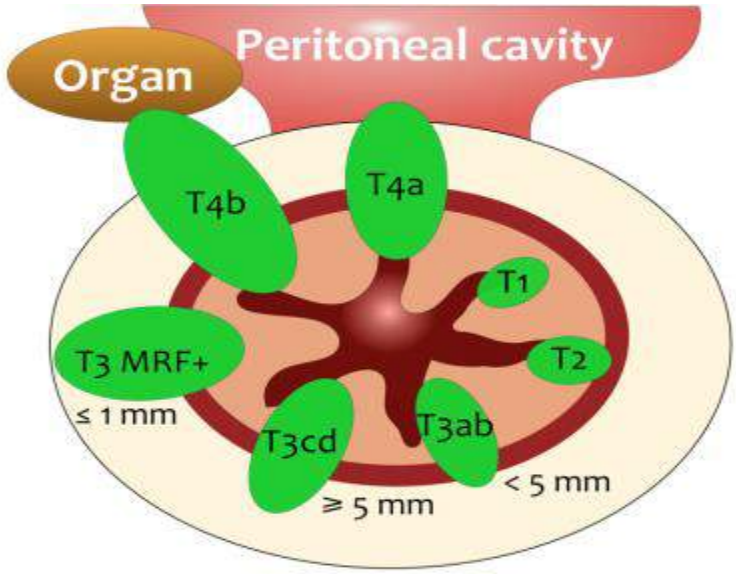


Figure 6- T staging of rectal cancer. T1 involves the mucosa and submucosa, T2 invade the muscularis propria, T3 invade the perirectal fat and T4 involve adjacent structures

Regarding N staging, N0 denotes no suspicious nodes, N1 1-3 nodes and N2 4 or more nodes. Size criteria was previously thought to be most important in determining malignant nodes with a cut off of 1 cm but signal heterogeneity and spiculation of borders has been found to be more relevant (23)(37)(42). The overall accuracy of nodal staging by MRI is low, with a sensitivity of 77% and specificity of 71% (23). Characterization may be enhanced by use of ultra-small superparamagnetic iron particles which has been shown to increase accuracy of MRI. These are absorbed by normal nodes making them T2 hypointense leaving pathologic nodes T2 hyperintense (43). Interestingly, restaging of nodes after chemoradiotherapy has been found to be more precise than primary staging of nodes (44).

Limitations exist to the use of the TNM system. Traditionally T and N stage were thought to be the main predictors of prognosis but some studies suggest that MRF involvement is more important (23)(42). The nodal status is not as important as the T status in patients who require surgery (23) and assignment of more importance to T status has been suggested (45). Moreover, CRM involvement in T2 tumors may be overstaged due to penetrating vessels as well as desmoplastic reaction (40). Staging done after chemoradiation therapy is less reliable; a study done in Germany found that MRF involvement tends to be overestimated (46). In addition, the lower third of the rectum is surrounded by little mesorectal fat making it difficult to determine CRM (24). It also does not adequately describe spread to adjacent organs such as surrounding bowel, ovaries and adnexa without the involvement of the peritoneum, all of which have an impact on overall prognosis and survival (47).

2.5. Rationale

New rectal cancer cases are on the rise. Important decisions are made based on the stage of the disease which is most accurately predicted by MRI (23). The preoperative stage determines whether or not neo-adjuvant therapy should be administered, the type of surgery to be done and any treatment required after surgery. It also predicts response to therapy, future recurrence and survival rates.

Owing to the complex nature of rectal anatomy, precision in imaging lies in the application of recommended protocols as regards to proper preparation of the patient as well as technical specifications in terms of magnetic field strength of the MRI machine, the sequences applied and the planes of imaging. No standardized imaging protocols exist in imaging of rectal cancer within the country. This is a baseline study done in Kenya; it may be used in the formulation of standardized MRI protocols to optimize RC imaging.

2.6. Questions

1. When the recommended imaging protocols are used, does the MRI stage match up to the postoperative histopathological stage of RC?
2. How accurate is MRI in T and N staging of RC?

2.7. Broad objective

To determine the imaging findings and staging accuracy of MRI in the local preoperative staging of rectal cancer in adult patients with pathology as the standard of reference.

2.8. Specific objectives

1. To evaluate the imaging findings of rectal MRI in the study population.
2. To establish the sensitivity and specificity of MRI in depicting depth of tumor spread and degree of metastatic adenopathy using histopathological diagnosis as the standard of reference.
3. To determine the sensitivity and specificity of MRI in determining CRM involvement using postoperative pathology findings as the gold standard.

CHAPTER 3: METHODOLOGY

3.1. Study design

Prospective analytic cross-sectional study

3.2. Study site

The study was done at two sites, Kenyatta National Hospital and Plaza Imaging Solutions. Kenyatta National Hospital (KNH) is situated along Hospital Road in Upper Hill, Nairobi. It is the main referral and teaching facility both in East and Central Africa attached to the University of Nairobi, College of Health Sciences. The hospital has an 1800 bed capacity with 22 outpatient clinics, 50 wards and 24 theatres and a casualty department. It is equipped with a 3T MRI machine that does an average of 150 MRIs per week.

Plaza Imaging Solutions is a premier imaging center located in General Accident House along Ralph Bunche Road, Nairobi. It is equipped with state of the art imaging equipment including a 1.5 T MRI and serves an average of 100 patients per week, most of whom are referred from consultant clinics. The center is managed by senior radiologists, graduate resident doctors from the University of Nairobi and radiographers.

3.3. Study population

The study included patients aged 18 years and above who have rectal cancer and have presented to the imaging centers for a preoperative MRI for purposes of staging.

3.4. Inclusion criteria

- Patients 18 years and above.
- Patients with histologically proven rectal carcinoma located within 15 centimeters from the anal verge as seen on colonoscopy.
- No contraindication to MRI which includes metal prostheses, pacemakers or prosthetic heart valves incompatible with MRI and allergies to contrast.

3.5. Exclusion criteria

- Pathology staging not required for management.
- Patients who have had surgery or other procedures that alter rectal anatomy.

- Patients who have received long course chemotherapy.
- Patients with known T and N stage who come for repeat imaging.

3.6. Sample size

A study done by Saklani A.P. et al (23) reported results of a meta-analysis of MRI staging of rectal cancer which revealed a sensitivity and specificity of T staging to be 87.0% (95% CI, 81.0 to 92.0) and 75.0% (95% CI, 68.0 to 80.0), therefore sample size was calculated using Buderer's formula:

$$n = \frac{Z^2{}_{1-\propto/2} x\ S_N(1 - S_N)}{L^2 x\ Prevalence}$$

Where,

n = Desired sample size

S_N = anticipated sensitivity set at 87.0%

S_p = anticipated specificity set at 75.0%

$Z_{1-\propto/2}$ = value from standard normal distribution corresponding to desired confidence level (Z=1.96 for 95% CI)

L = absolute precision desired on either side (half – width of the confidence interval) of sensitivity which will (92.0 - 81.0) / 2 = 5.5%

L = absolute precision desired on either side (half – width of the confidence interval) of specificity which will (80.0 - 68.0) / 2 = 6.0%

The prevalence of rectal carcinoma among Kenyan patients is 3% (2).

Sensitivity:

$$n = \frac{1.96^2 x\ 0.87(1-0.87)}{0.055^2 x\ 0.03} = 4788$$

Specificity:

$$n = \frac{Z^2{}_{1-\propto/2}\ x\ S_p\ x\ (1-S_p)}{L^2\ x\ (1-Prevalence)}$$

$$n = \frac{1.96^2\ x\ 0.75\ x\ (1-0.75)}{0.06^2\ x\ (1-0.03)} = 204$$

On average, KNH and Plaza Imaging Centre report a total of 12 rectal MRIs that have been ordered for staging purposes. The study duration is 4 months.

Adjusting the sample size for finite populations less than 10,000 (for SENSITIVITY)

$$nf = \frac{n_0}{1+\frac{n_0-1}{N}} = \frac{4788}{1+\frac{4788-1}{48}} = 48$$

Adjusting the sample size for finite populations less than 10,000 (for SPECIFICITY)

$$nf = \frac{n_0}{1+\frac{n_0-1}{N}} = \frac{204}{1+\frac{204-1}{48}} = 39$$

Sample size =48

3.7. Sampling technique

Convenience sampling was used.

3.8. Variables

- Demographics- Age and sex of patient
- Imaging characteristics of the tumor
- Location of tumor- Lower, mid or upper third
- Depth of tumor invasion and T stage
- MRF and CRM involvement
- Nodal metastases and N stage

3.9. Procedures

Patients' age, sex and clinical information was reviewed to confirm whether or not a pelvic MRI is indicated for suspected RC. These indications include definitive diagnosis of rectal cancer, assessment of local extent of disease and evaluation of local recurrence. Eligibility for the study was then assessed using the inclusion and exclusion criteria earlier outlined and consent will be sought. MRI was done in accordance to standard imaging protocol for imaging RC adapted from the MERCURY study (38)(Appendix I) using a Phillips achiever D stream 1.5T machine at Plaza Imaging solutions or a Phillips Ingenia 3T machine at KNH and reported by two independent radiologists who assigned a T and N stage based on imaging. Any difference between the two radiologists was resolved by consensus.

The surgeries were done within 1 month of imaging at Kenyatta National Hospital by a general surgeon. The resection biopsy was then put in 10% formalin and handed over to the pathology department, where grossing of the specimen was done and the tissue was put in cassettes and Hematoxylin and Eosin staining done. The cassettes were then put in wax and frozen. Subsequently, the tissue was shaved using a microtome and put in a water bath to remove the wax. It was then scooped from the bath using a slide, mounted with a cover slip then dried. The biopsy was then examined under microscopy by two independent pathologists who were blinded to the MRI stage. Differences in staging was also resolved by consensus.
The MRI stage was then correlated with the pathological stage to check for accuracy of imaging.

Study flow chart

Patient presents for pelvic MRI (Indicated as described above)

Assessment of eligibility for the study as per the inclusion and exclusion criteria

Informed consent obtained and enrolment into study

MRI done as per protocol, interpretation of study and assignment of T and N stage

Surgery done and pathological specimen obtained

Specimen processed by pathology and T and N stage assigned

Comparison of imaging and pathological T and N stage by principal investigator

3.10. Data management

Data generated was imported from the data collection form into Microsoft Excel. It was checked for completeness prior to entry into SPSS Statistics version 21 for analysis. Demographic characteristics of the patients was analyzed and presented as frequencies and proportions and as means with standard deviations if data collected is normally distributed or medians with interquartile range if data is not normally distributed. Tumor location, invasion, CRM involvement and nodal status as seen on MRI and proportion correlating with histopathology findings were analyzed and presented as frequencies and proportions. 2x2 tables were then generated and sensitivity, specificity, positive predictive value, negative predictive values and accuracy of the study variables calculated.

Data was protected by use of passwords. Only the statistician and principal investigator had access to the data.

3.11. Ethical consideration

This proposal was submitted to the Kenyatta National Hospital University of Nairobi (KNH-UON) Ethics and Research Committee for approval. Permission to conduct the

study was obtained from The Director, Plaza Imaging Solutions and the Head of the KNH radiology department.

Informed and signed consent was obtained from each participant after explaining to them what the study entails as well as its risks and benefits. Participation was voluntary. Information was kept confidential.

3.12. Study results dissemination plan

Results of the study will be presented to the Department of Diagnostic Imaging and Radiology Medicine and Plaza Imaging Solutions as well as the KNH radiology, surgery and pathology department. This will hopefully encourage multidisciplinary management with resultant better outcomes. Publication in a peer reviewed journal will also be sought.

Work plan

ACTIVITY	**APRIL-SEPTEMBER 2020**	**OCTOBER 2020-JANUARY 2021**	**FEBRUARY-APRIL 2021**
Proposal development			
Proposal correction and ethical approval			
Data collection and analysis			
Report writing			
Result dissemination and publication			

Budget

ITEM	Description	Kshs
Ethical approval	Submission to KNH-UON ERC committee	2000
Supplies	Draft proposal printing, 36 pages, 1 copy @Ksh 10 per page	360
	Draft proposal photocopying, 36 pages, 2 copies @ Ksh 5 per page	360
	Final proposal printing, 36 pages, 1 copy @ Ksh 10 per page	360
	Final proposal photocopying, 36 pages, 2 copy @ Ksh 5 per page	360
	Data collection tool printing, 3 pages,1 copy @ Ksh 10 per page	30
	Data collection tool photocopying, 3 pages, 35 copies @ Ksh 5 per page	525
	Final report printing: 100 pages, 1copy @ Ksh 10 per page	1000
	Final report photocopying: 100 pages, 3 copies @ Ksh 5 per page	1500
	Final report binding:4 reports @ Ksh 2000	8000
	Stationery (pens, pencils)	1000
Personnel	Data clerk/statistician	25000
Contingency	10% of total cost	3950
Total		**43445**

The study participants paid for their MRI as well as their pathology staging. No financial incentive was offered to them for participation in the study. The study participants had improved turnaround times as well as more precise imaging and pathologic staging.

CHAPTER 4: RESULTS

A total of 48 patients, 22 (45.8%) male and 26 (54.2%) female took part in the study. A Shapiro- Wilks test of normality showed that the data was normally distributed (p=0.436), therefore the mean is reported. The mean age of the patients was 52.3 years (SD 14.1). The youngest patient was 18 years while the oldest was 79 years of age.

The rectal tumors were well demonstrated on the MRI images. The average distance of the tumors from the anal verge was 3.6 cm. They were located at different sites in the rectum as shown on Table 1 and were most commonly located in the lower third in 35 (72.9%) of patients.

Table 1- Location of the rectal tumors from the anal verge

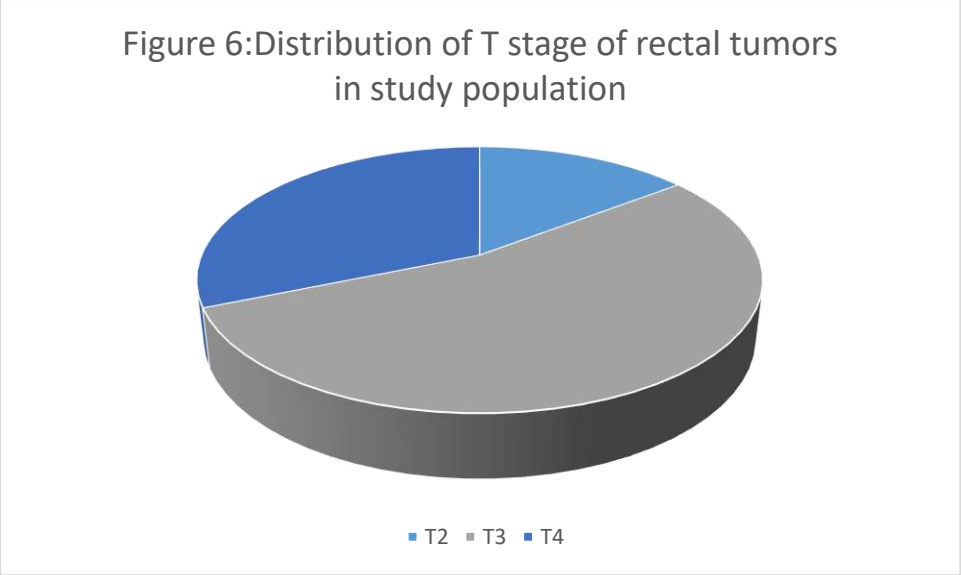
Tumor location	**N (%)**
Lower third(less than or equal to 5.0 cm above the anal verge)	**35 (72.9%)**
Middle third (More than 5.0 cm to less than or equal to 10cm above the anal verge)	**9 (18.8%)**
Upper third (More than 10 cm above the anal verge)	**4 (8.3%)**

Regarding the signal intensity of the tumors, 40 (83.3%) were of intermediate signal intensity, defined in the rectum as signal between that of the muscularis propria that is hypointense and the mucosa that is hyperintense. 8 (16.7%) were predominantly hyperintense.

EMVI, which is described as the presence of RC tumor cells in the vessels beyond the muscularis propria with subsequent vascular dilatation equal to or more than 3 millimeters, was seen in 11/48 patients (22.9%).

3.1. T staging

Histopathology revealed that early intramural T1/T2 tumors were found in 7 patients (14.6%), T3 in 26 patients (54.2%) and T4 in 15 patients (31.2%) (Figure 6).



Extent of invasion of the rectal wall by tumor was correctly evaluated by MRI in 6/7 of T1/T2 lesions (85.7%), 24/26 of T3 lesions (92.3%) and 14/15 of T4 lesions (93.3%). Two by two tables showing the imaging and pathologic T staging are provided below (Table 2, 3)

Table 2: Summary of imaging and pathologic findings of early, low risk (T1/T2) tumors and high risk (T3/T4) tumors.

	Histology T3/T4	Histology T1/T2	Total
MR T3/T4	38	1	39
MR T1/T2	3	6	9
Total	41	7	48

The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of MRI in the T staging of rectal tumors were 92.6%, 85.7%, 97.4%, 66.7% and 91.8%.

3.2. Mesorectal fascia status

The MRF was well depicted on MRI as a pencil-thin T2 low signal intensity structure surrounding the perirectal fat and enveloping the mesorectum. It was evaluated in T3 tumors and was breached in 7 patients evidenced in histopathology as tumor invasion into the MRF (Table 3). The accuracy of MRI in predicting mesorectal fascia involvement was 92%. The sensitivity, specificity, PPV and NPV were 85.7%, 94.7%, 85.7% and 94.7% respectively.

Table 3: MRF involvement: Imaging and pathology findings.

	Histology MRF+	Histology MRF-	Total
MR MRF+	6	1	7
MR MRF-	1	18	19
Total	7	19	26

3.3. Circumferential resection margin

Circumferential resection margin involvement was evaluated on MRI and defined as tumor within 1mm of the mesorectal fascia. It has been shown to predict tumor recurrence and is therefore an important component in rectal cancer imaging. MRI correctly predicted CRM involvement in 10 out of 12 of the T3 lesions (Table 4). The sensitivity, specificity, PPV and NPV and accuracy were 83.3%, 92.9%, 90.9%, 86.6% and 88% respectively.

Table 4: CRM involvement: Imaging and pathology findings.

	Histology CRM+	Histology CRM-	Total
MR CRM+	10	1	11
MR CRM-	2	13	15
Total	12	14	26

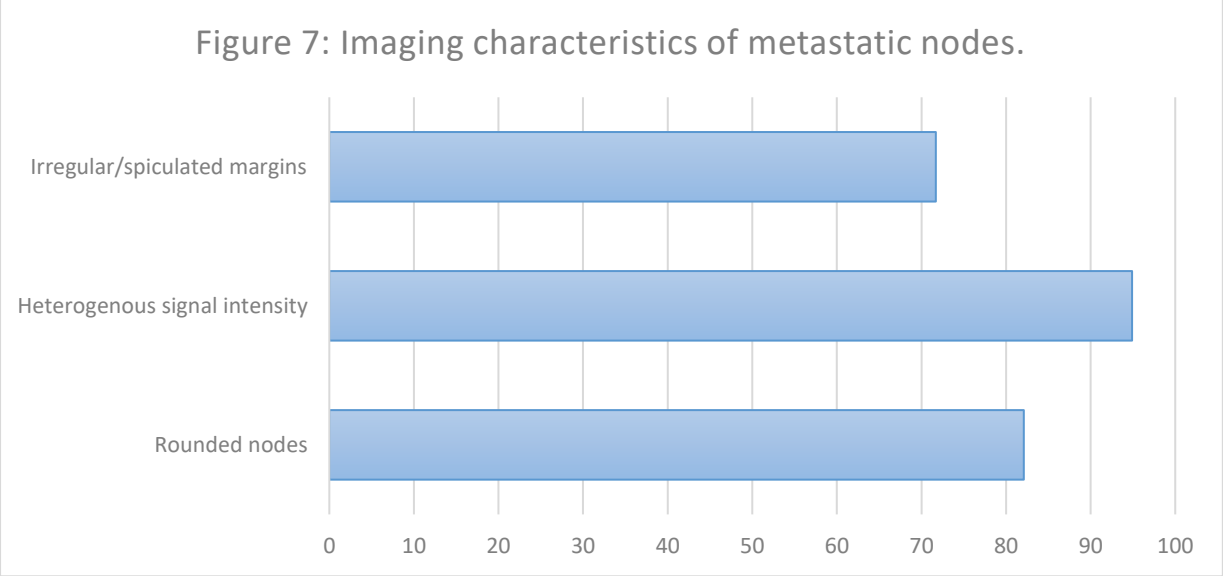
3.4. N staging and nodal imaging characteristics

All the pathological specimens that demonstrated nodal involvement had adequate nodal sampling, defined as 12 or more nodes. Altogether 30 (62.5%) patients had metastatic nodal involvement on histopathology: 20 were staged as pT1 (66.7%) and 10 were staged as pT2 (33.3%). The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of MRI in the N staging of rectal tumors were 80.0%, 55.5%, 75.0%, 62.5% and 70.8% (Table 5).

Table 5: Summary of imaging and pathologic findings of metastatic nodal involvement

	Histology Node +	Histology Node -	Total
MR Node +	24	8	32
MR Node -	6	10	16
Total	30	18	48

Regarding imaging characteristics of the nodes in different patients, 25/30 (82.1%) of the nodes were rounded, 29/30 (94.9%) had heterogeneous signal intensity and 22/30 (73.3%) had irregular or spiculated margins (Figure 7).



CHAPTER 5: DISCUSSION.

This study presents an assessment of the precision of MRI as a preoperative staging tool in rectal cancer. Staging at presentation determines patient management, risk of tumor recurrence and is of prognostic value. The purpose of this study was to determine the diagnostic accuracy of MRI in the preoperative staging of rectal cancer in adult patients with pathology as the gold standard.

5.1. Demographics and imaging characteristics

In our study, the mean age of the patients was 52.3 years. This is comparable to the mean age in the study by Algebally et al (41), which was 50 years. It is significantly lower than that of the MERCURY group, which was 62 years (38). The difference is probably because their study comprised of a larger number of patients. We found that RC is more common in females (54.2%), which disagrees with the findings of Hassan et al (29) as well as Brown et al (38),whose studies also found that RC occurs more frequently in male patients. There is however no known significant gender predilection of RC (48).

Most of the tumors were located in the lower third of the rectum (72.9%), which is consistent with the findings of Rania et al (49), who stated that RC occurs most frequently in the lower third of the rectum in 67.6% of cases. Khan et al (50) found that cancers in the lower third more commonly require neoadjuvant therapy, are less likely to have restorative surgery and have higher rates of CRM involvement on pathologic evaluation.

While pathologic sampling remains the gold standard in determining tumor histology, MRI can attempt to predict this based on the signal intensity of the tumor. Adenocarcinomas are typically of intermediate signal intensity on T2 MRI studies while mucinous tumors are hyperintense (40). In our study, most tumors were of intermediate signal (83.3%) in keeping with adenocarcinoma. Hyperintense signal was seen in 16.7% of cases suggesting mucinous histopathology. 5-15% of RC tumors are known to be mucinous (51), which is comparable to our findings. They are more likely to metastasize and are often of advanced stage when diagnosed, with overall poor prognosis (40).

EMVI was detected in 22.9% of patients. Unfortunately, we were unable to determine the precision of MRI in predicting EMVI because it is not included in the standard histopathology reports. Its presence is linked to higher rates of recurrence and mortality in RC but is not considered when planning treatment (52).

5.2. T-Staging

In our study, 14.6% of tumors were T1/T2 (Figure 8), 54.2% of tumors were T3 (Figure 12, 13, 15) and 31.2% of tumors were T4 (Figure 9, 10). The predominant stage at presentation was T3, which agrees with the finding of Brown et al (38) and Hassan et al (29). However in both studies, there were more T1/T2 tumors and less T4 tumors. The advanced stage at presentation in our study may be attributed to the health seeking behavior of the patients as well as the delays in diagnostics, referral and instituition of management in low and middle income countries, which has been described by Tiwari et al (53). The T staging was correctly evaluated in 91.8% of the cases, which is in concordance with the findings of Algebally et al (41), who found an accuracy of 85.7% for MRI in assessment of the depth of extension of rectal tumor. The sensitivity, specificity, PPV and NPV in our study was 92.6%, 85.7%, 97.4% and 66.7%. The high accuracy, sensitivity, specificity and PPV are consistent with a number of studies (23)(41)(39). The differentiation of T2 from early T3 tumors is a known limitation in rectal cancer imaging due to the inability to distinguish mesorectal fascia invasion from desmoplastic reaction (40) (Figure 11).

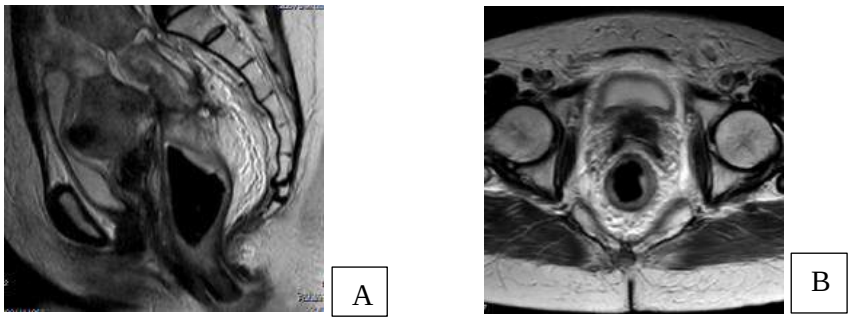


Figure 8:Pathologically proven T2 rectal cancer in a 49 year old man involving the low and mid rectum. The tumor does not extend beyond the hypointense muscularis propria. No mesorectal adenopathy was seen. The presacral space was also noted to be thickened in this patient.

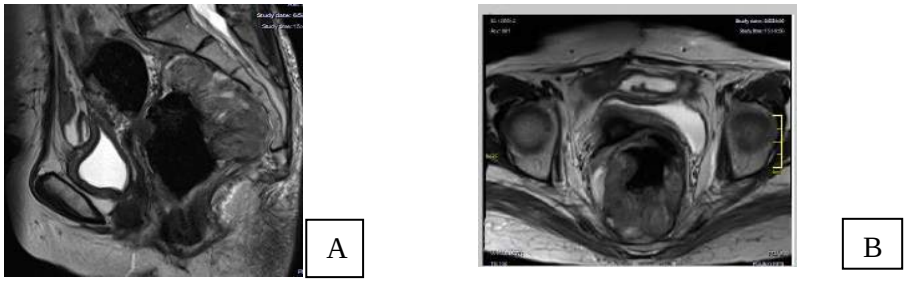


Figure 9: Advanced T4b mid rectal tumor seen to extend to the upper third of the rectum. Sagittal (A) and axial (B) images show a fleshy mass in the 2 to 10 o clock position invading the presacral space. No bony involvement was noted.

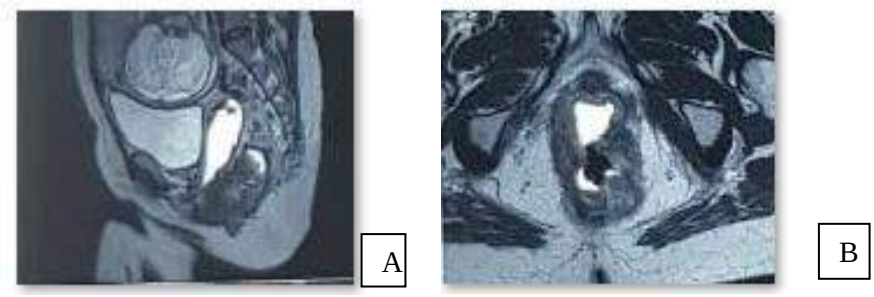


Figure 10: T4b rectal tumor in a 35 year old lady. The tumor involves the lower third of the rectum (A) and is seen to extend anteriorly into the vagina, with formation of a rectovaginal fistula (B). The patient was also 30 weeks pregnant.

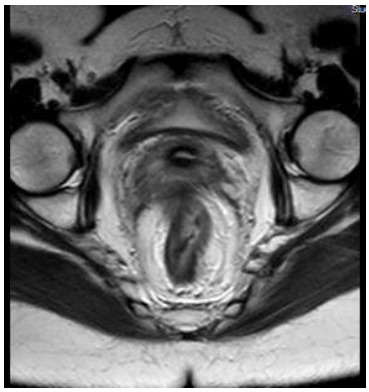


Figure 11: Low rectal mass in a 39 year old woman. It was designated a T stage of T2 with desmoplastic reaction. Pathology showed a T3 lesion. No metastatic lymph nodes were demonstrated both on imaging and pathology.

5.3. Involvement of MRF

MRF involvement was correctly depicted in MRI in 6/7 patients, with an overall accuracy of 92%. The sensitivity, specificity, PPV and NPV were 85.7%, 94.7%, 85.7% and 94.7%. These findings are similar to those of Hassan et al (29), who reported a sensitivity, specificity, PPV and NPV of 90%, 90%, 72% and 93.1%. One false positive was found in a patient with an anterior rectal tumor (Fig 12). Limitations in MRF assessment in anterior rectal tumors have

been documented in literature and are thought to be due to the thin anterior perirectal fat which makes it harder to demonstrate the anterior MRF as well as the denonvillers fascia (54).

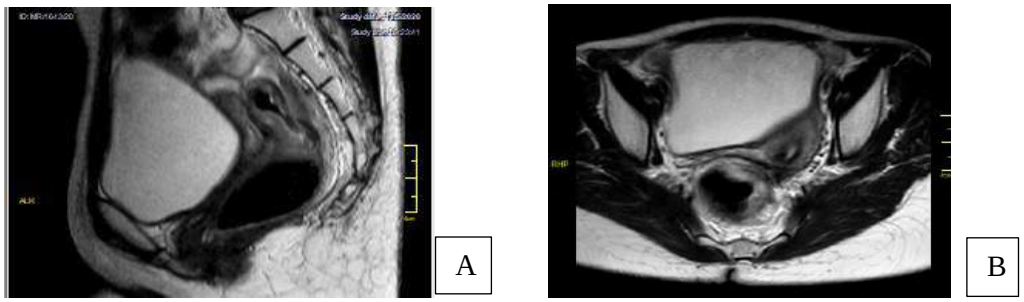


Figure 12: High anterior rectal tumor in a 56 year old man. Axial images show irregular wall thickening at the 11 to 5 o clock position. The tumor is staged at T3 with breech of the MRF seen at the 12 o clock position. Histopathology showed no involvement of the MRF in this specimen.

5.4. CRM involvement

Tumor involvement of the circumferential resection margin was accurately reported in 10/12 patients, with an accuracy of 88%. The sensitivity, specificity, PPV and NPV were 83.3%, 92.9%, 90.9% and 86.6%. This is in line with the study by Algebally et al (41), whose specificity, sensitivity, PPV, NPV and accuracy were 84.6%, 97.6%, 91.4%, 94.6% and 94.6%. One false negative was seen in an anterior rectal tumor, which may also be attributed to the thin mesorectal fat. One positive was noted in a low rectal tumor, likely due to the tapering of the rectal and perirectal tissue (Figure 13).

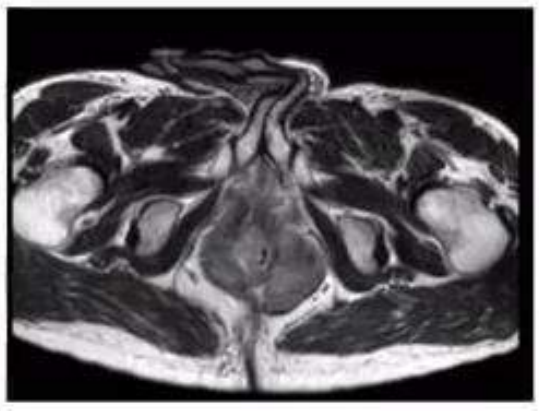


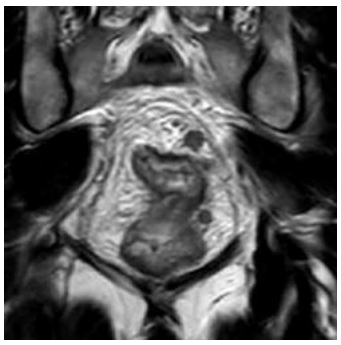
Figure 13: Low rectal tumor in a 33 year old man with a prominent exophytic component staged at T3. The circumferential resection margin was thought to have been involved by tumor. Pathology however reported that the tumor was CRM negative

5.5. Assessment of nodal metastases

In our study, 30/48 (62.5%) of patients had metastatic nodal involvement. 66.7% were staged as N1 pathologically while 33.3% were staged as N2. The sensitivity, specificity, PPV, NPV and accuracy were 80.0%, 55.5%, 75.0%, 62.5% and 70.8%. Our findings are different from those of Chatterjee et al (55) who found a sensitivity, specificity, PPV and NPV of 100%,

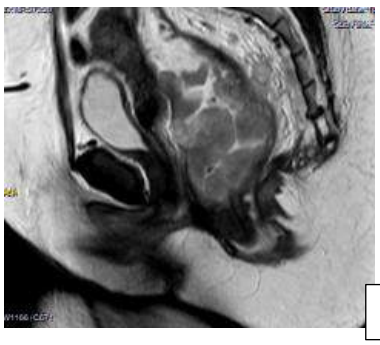
78.3%, 77.3% and 100%, and Algebally et al (41), who found that the sensitivity, specificity, PPV, NPV and accuracy of MRI in nodal staging was 82.1%, 75%, 67.3%, 60% and 86.1% respectively. Both studies used size criteria to determine whether nodes were metastatic, while we used morphologic characteristics which has been shown to be a better predictor of nodal status. Wide variability in the accuracy of MRI has been reported in literature, ranging from 39% to 95% (36).

As regards the nodal characteristics, 82.1% of the nodes were rounded, 94.9% had a heterogenous internal signal while 71.7% had irregular or spiculated margins. The margins of the nodes as well as its internal signal characteristics are more accurate than the size of the differenciating benign from malignant nodes (Figure 14, 15).



A

Figure 14: Coronal T2W MRI images in a 45 year old man demonstrating metastatic nodal involvement. Two nodes are seen within the mesorectal fat. Both nodes are rounded with heterogenous signal intensity. The larger node located superiorly also has spiculated margins.



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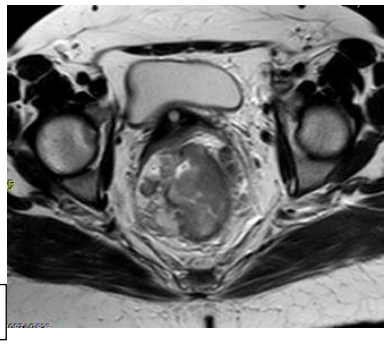

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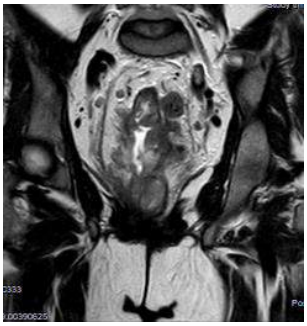

C

Figure 15: T3N2 Fleshy rectal tumor in a 64 year old man involving the lower and middle rectum with extensive nodal involvement. Multiple rounded mesorectal nodes of various sizes are noted. The nodes have heterogenous signal intensity and have ill-defined, spiculated margins, in keeping with metastatic nodal involvement.

5.6. Study limitations

Our study is limited by its small sample size. We also couldn't look at the diagnostic accuracy of MRI in assessment of EMVI because we realized that local histopathology protocols do not report EMVI and we therefore wouldn't have a reference test.

CONCLUSION

Our study found that MRI has a high diagnostic accuracy comparable to other previous studies carried out in more developed countries in the determination of depth of extramural spread of rectal tumors, evaluation of MRF involvement and the circumferential resection margin as well as assessment of metastatic nodal involvement.

RECOMMENDATIONS

MRI should be the cornerstone in the local staging of RC. Standardized imaging protocols should be used when imaging RC to ensure high diagnostic accuracy. EMVI assessment should be embraced in standard RC pathology reporting. Processing and reporting of histology specimens should be standardized. Multidisciplinary management of RC should be adopted: interactions between surgeons and radiologists involved in RC imaging should be encouraged so that imaging directs intraoperative nodal harvesting and radiology and pathology workshops in RC imaging and histopathology reporting should be conducted. Information management systems that integrate clinical, radiologic and pathologic information should be set up to encourage future studies in oncologic imaging.

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APPENDIX I- DATA COLLECTION FORM

Participant code: _____
Age: _____
Sex: _____

MRI Findings

I- Distance from anal verge: [] cm

II- Craniocaudal length: [] cm

III- Imaging characteristics

T1- _____

T2- _____

IV- MR-T category:

☐Tx ☐T1/2 (tumor confined to rectal wall)
☐T3a (tumor penetrates < 1 mm beyond muscularis propria)
☐T3b (tumor penetrates 1- 5 mm beyond muscularis propria)
☐T3c (tumor penetrates >5-15 mm beyond muscularis propria)
☐T3d (tumor penetrates > 15 mm beyond muscularis propria)
☐T4a (tumor penetrates through surface of anterior peritoneal reflection)
☐T4b (tumor invades or adherent to adjacent organs or structures)

V- EMVI:

☐Absent ☐ Present

VI- CRM (for T3 only):
Shortest distance of tumor to MRF (or anticipated CRM): [ ] mm

VII- Lymph node involvement*:

☐ N0 (no nodes)
☐ N1 (1-3 nodes)
☐ N2 (4 or more nodes)

*Suspicious morphologic criteria: (1) round shape, (2) irregular borders, (3) heterogeneous signal intensity

IMPRESSION:

Stage: T [ ] N[ ]
CRM: ☐clear ☐ threatened ☐involved

Histopathology findings

I-Distance from anal verge: [] cm

II-Craniocaudal length: [] cm

I- MR-T category:

☐Tx ☐T1/2 (tumor confined to rectal wall)
☐T3a (tumor penetrates < 1 mm beyond muscularis propria)
☐T3b (tumor penetrates 1- 5 mm beyond muscularis propria)
☐T3c (tumor penetrates >5-15 mm beyond muscularis propria)
☐T3d (tumor penetrates > 15 mm beyond muscularis propria)
☐T4a (tumor penetrates through surface of anterior peritoneal reflection)
☐T4b (tumor invades or adherent to adjacent organs or structures)

II- For low rectal tumors:

- Invasion of anal sphincter complex:

☐Absent ☐Invades internal sphincter (IS) only
☐Invades IS and extends into intersphincteric space (ISS)
☐Invades IS + ISS + extends into or through external sphincter

III- CRM (for T3 only):
Shortest distance of tumor to MRF (or anticipated CRM): [ ] mm

Number of nodes sampled: _____

IV- Lymph node involvement*

☐ N0 (no nodes)
☐ N1 (1-3 nodes)
☐ N2 (4 or more nodes)

*Suspicious morphologic criteria: (1) round shape, (2) irregular borders, (3) heterogeneous signal intensity

IMPRESSION:

Stage: T [ ] N[ ]
CRM: ☐clear ☐ threatened ☐involved
Sphincter involvement: ☐No ☐Yes

APPENDIX II- MRI protocol for rectal cancer

Patient preparation

1. Patient should empty bladder before imaging
2. Sedation (0.3 to 0.35 mg/kg IV once, administered over 20 to 30 seconds) and analgesia (IM Diclofenac 50mg) may be given if patient is overly anxious or in pain.

Administration of bowel enema, distention of rectal lumen and bowel contrast not necessary.

External pelvic phased array coil should cover from the level of the aortic bifurcation to the anal verge. Endorectal coil should **NOT** be used.
Scanning plane: Perpendicular to the MRF
Scanning protocol

	AXIAL T1 FSE	**AXIAL T2 FSE**	**SAG T2 FSE**	**CORONAL T2 FSE**
Repetition time (ms)	360	3320	3500	3500
Echo time (ms)	10	90	90	90
Echo train length	25	25	25	
Number of slices	25	40	28	25
Field of view (mm)	240	240	250	250
Slice thickness	3	3	3	3
Slice gap (mm)	1	1	1	1
Matrix	250 X 250	250 X 250	250 X 250	250 X 250
Acquisition time (min)	5.5	5.5	4	4

Appendix IIIa: Information and Consent Form – ENGLISH
INFORMATION AND CONSENT FORM
STUDY TITLE: Preoperative Local Staging of Rectal cancer Using Magnetic

Resonance Imaging with Pathologic Correlation in Kenyan Patients.

Kenyatta National Hospital, Nairobi, Kenya

Plaza Imaging Centre, Nairobi, Kenya

Principal Investigator: Dr. Fiona Achieng' Anyumba (Mmed student, University of Nairobi)
Co-Investigators: Dr. Alfred Odhiambo (University of Nairobi), Dr. Timothy Mutala (University of Nairobi), Dr. Wairimu Waweru (University of Nairobi) and Dr. Jane Mugure (University of Nairobi).

Introduction:

I would like to tell you about a study being conducted by the above-listed researchers. The purpose of this consent form is to give you the information you will 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, what happens if you participate in the study, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions to your satisfaction, you may decide to be in the study or not. This process is called 'informed consent.' Once you understand and agree to be in the study, I will request you to sign your name on this form. You should understand the general principles which apply to all participants in a medical research: i) Your decision to participate is entirely voluntary ii) You may withdraw from the study at any time without necessarily giving a reason for your withdrawal iii) Refusal to participate in the research will not affect the services you are entitled to in this health facility or other facilities. We will give you a copy of this form for your records.

May I continue? YES / NO

WHAT IS THIS STUDY ABOUT?

The researchers listed above are conducting a research on the accuracy of magnetic resonance imaging in staging rectal cancer before surgery. The aim of the research is to validate MRI as the primary imaging modality in the assessment of rectal cancer. Approximately 33 patients will be selected for this study. We are asking for your consent to consider participating in this study.

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

If you agree to participate in this study, the following things will happen:

- You will undergo an MRI study to determine the rectal cancer stage
- After surgery, the specimen will be analyzed by pathologists to check the pathological stage
- The MRI and pathological stage will be compared to assess how accurate MRI is in determining the status of rectal cancer.

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

Medical research has the potential to introduce psychological, social, emotional and physical risks. Effort should always be put in place to minimize the risks. One potential risk of being in the study is the loss of privacy. We will keep everything you tell us as confidential as possible. We will use a code number to identify you in a password-protected computer database and will keep all of our paper records in a locked file cabinet. However, no system of protecting your confidentiality can be absolutely secure, so it is still possible that someone could find out you were in this study and could find out information about you.

ARE THERE ANY BENEFITS BEING IN THIS STUDY?

You may not benefit directly as an individual, but the study will aid in development of standardized imaging protocols which are pivotal in imaging of rectal cancer. There will be no direct compensation for participating in this study.

WILL BEING IN THIS STUDY COST YOU ANYTHING?

Participation is free and voluntary.

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

There is no expense involved in participating in this study. You will not be compensated.

CONTACTS: WHAT IF YOU HAVE QUESTIONS IN FUTURE?

If you have further questions or concerns about participating in this study, please call or send a text message to the Principal Investigator, Dr. Fiona Anyumba, 0722334148.
For more information about your rights as a research participant, you may 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 participate in research is voluntary. You are free to decline participation in the study, and you can withdraw from the study at any time without suffering any negative consequences. You will continue to receive the care and treatment needed even if you do not wish to participate in this study.

CONSENT FORM (STATEMENT OF CONSENT)
Participant's statement

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counselor. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw at any time. I freely agree to participate in this research study.
I understand that all efforts will be made to keep information regarding my identity confidential.
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

Participant printed name: _____

Participant signature / Thumb stamp _____ Date _____

Researcher's statement

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

Researcher's Name: **_____ Date**: **_____**

Signature _____

Role in the study: **_____**

Witness (*If witness is necessary, a witness is a person mutually acceptable to both the researcher and participant*)
Name _____

Contact information _____

Signature /Thumb stamp: _____
Date: **_____**

Appendix IIIb: Information and Consent Form – SWAHILI
MAELEZO KUHUSU UTAFITI/WARAKA WA IDHINI

STUDY TITLE: Preoperative Local Staging of Rectal cancer Using Magnetic

Resonance Imaging with Pathologic Correlation in Kenyan Patients.

Kenyatta National Hospital, Nairobi, Kenya

Plaza Imaging Centre, Nairobi, Kenya

Mtafiti mkuu: Dkt. Fiona Anyumba (Chuo Kikuu cha Nairobi)

Watafiti weza: Dkt. Alfred Odhiambo (University of Nairobi), Dkt. Timothy Mutala (University of Nairobi), Dkt. Wairimu Waweru (University of Nairobi), Dkt. Jane Mugure (University of Nairobi).

UTANGULIZI

Ningependa kukueleza juu ya utafiti unaofanywa na watafiti waliotajwa hapo juu. Madhumuni ya fomu hii ya idhini ni kukupa maelezo unayohitaji ili kukusaidia uamuzi ikiwa Utahusishwa kwa utafiti huu au la. Jisikie huru kuuliza maswali yoyote kuhusu madhumuni ya utafiti, kinachotokea ikiwa unashiriki katika utafiti, hatari na faida iwezekanavyo, haki zako kama kujitolea, na kitu kingine chochote kuhusu utafiti au fomu hii ambayo haijulikani. Tunapojibu maswali yako yote kwa kuridhika kwako, unaweza kuamua kuwa katika utafiti au la. Utaratibu huu unaitwa 'kibali cha habari'. Mara unapoelewa na kukubali kuwa katika utafiti, nitakuomba kusaini jina lako kwenye fomu hii. Unapaswa kuelewa kanuni za jumla ambazo zinatumika kwa washiriki wote katika utafiti wa matibabu: i) Uamuzi wako wa kushiriki ni kikamilifu kwa hiari ii) Unaweza kujiondoa kwenye utafiti wakati wowote bila ya kutoa sababu ya uondoaji wako iii) Kukataa kushiriki katika utafiti hauathiri huduma unazostahili kwenye kituo hiki cha afya au vifaa vingine. Tutakupa nakala ya fomu hii kwa rekodi zako.

Naweza kuendelea? NDIO/LA

UTAFITI HUU UNAHUSU NINI?

Mtafiti aliotajwa hapo juu atawaoji watu ambao wanafanyiwa uchunguzi wa MRI. Lengo la utafiti ni kutambua usahihi wa MRI kwa kuonyesha jinsi saratani ya puru imeenea. Karibu wagonjwa 33 watashiriki katika utafiti huu. Tunaomba ridhaa yako kufikiria kushiriki katika utafiti huu.

NI NINI KITAKACHO FANYIKA UKIAMUA KUHUSIKA KWA UTAFITI HUU?
Ikiwa unakubali kushiriki katika utafiti huu, mambo yafuatayo yatatokea:

- Utapigwa picha ya MRI kuangalia uenezi wa saratani
- Baada ya upasuaji, kiolezo kitapimwa pia kuangalia jinsi saratani imeenea
- Majibu ya MRI na kiolezo yatalinganishwa kudhibiti usahihi wa MRI.

KUNA MADHARA YOYOTE YANAYOTOKANA NA UTAFITI HUU?
Utafiti wa matibabu una uwezo wa kuanzisha hatari za kisaikolojia, kijamii, kihisia na kimwili. Jitihada zinapaswa kuwekwa daima ili kupunguza hatari. Hatari moja ya kuwa katika utafiti ni kupoteza faragha. Tutaweka kila kitu unachotuambia kama siri iwezekanavyo. Tutatumia namba ya nambari ili kukutambua kwenye darasani ya kompyuta iliyohifadhiwa na nenosiri na tutahifadhi rekodi zote za karatasi kwenye baraza la mawaziri lililofungwa. Hata hivyo, hakuna mfumo wa kulinda siri yako inaweza kuwa salama kabisa, kwa hiyo bado inawezekana

kwamba mtu anaweza kujua wewe ulikuwa katika utafiti huu na anaweza kupata habari kukuhusu.

KUNA MANUFAA YOYOTE KWA KUHUSIKA KWA UTAFITI HUU?
Huwezi kufaidika moja kwa moja kama mtu binafsi, lakini utafiti huu utasaidia katika uteuzi utaratibu na mpangilio wa kufanya MRI kwa kupima saratani ya puru kabla ya upasuaji. Hutakuwa na fidia moja kwa moja ya kushiriki katika utafiti huu.

KUHUSIKA KWA UTAFITI HUU KUTAGHARIMIA CHOCHOTE?

Hakuna malipo ila tutachukua muda wa dakika kumi

UTAPATA MALIPO YOYOTE AU FIDIA

Hakuna malipo au fidia ili kuhusika kwa utafitu huu

UKITAKA KUULIZA SWALI BAADAYE KUHUSU UTAFITI HUU?

Wasiliana na Mtafiti mkuu, Daktari Fiona Anyumba kwa nambari ya simu: +254 722334148 Ama mwenyekiti au katibu msimamizi, utafiti, Hospitali ya Kitaifa ya Kenyatta na Chuo kikuu cha Nairob kupitia nambari 2726300/44102; au kwa anuani uonknh_erc@uonbi.ac.ke. Watafiti watakurejeshea pesa zilizotumika kwa mawasiliano kuhusu utafiti huu.