BLADDER PROTOCOL COMPLIANCE AND ITS EFFECT ON RADIATION ENTERITIS AMONG CERVICAL CANCER PATIENTS AT OCEAN ROAD CANCER INSTITUTE

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By

Mwitasrobert Gisiri

A Dissertation Submitted in (Partial) Fulfillment of the Requirements for the Degree of Masters of Medicine in Clinical Oncology of The Muhimbili University of Health and Allied Sciences

October, 2024

CERTIFICATION

The undersigned certify that they have read and hereby recommend for the ***acceptance, by the Muhimbili University of Health and Allied Sciences this research project entitled, "BLADDER PROTOCOL COMPLIANCE AND ITS EFFECT ON RADIATION ENTERITIS AMONG CERVICAL CANCER PATIENTS AT OCEAN ROAD CANCER INSTITUTE."***, in (Partial) fulfillment of the requirements for the degree of Masters of Medicine in (Clinical Oncology) of the Muhimbili University of Health and Allied Sciences.

_____

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(Supervisor)

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Date:

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Dr. Sikudhani Muya

(Co-Supervisor)

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Date:

DECLARATION AND COPYRIGHT

I, **Mwitasrobert Gisiri**, hereby declare that this research project is my original work and that it has not been presented and will not be presented to any other university for a similar or any other degree award.

Signature: ……. Date: …….…….

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ACKNOWLEDGEMENTS

My dear appreciation goes to my family for their unwavering support throughout the entire journey

I also recognize the efforts of my supervisors, Dr. Christina Malichewe and D.r Sikudhani Muya, in providing guidance and mentorship in every stage of this project.

I thank God the Almighty for his abundant grace and blessings in all endeavors leading to this day.

DEDICATION

This study is dedicated to my entire family. I can't thank them enough for being there both physically and in prayer. I am forever grateful.

ABSTRACT

Background: Cervical cancer is the 4th most common cancer in women worldwide and a leading cause of cancer morbidity in Tanzania. Radiotherapy is the primary treatment for locally advanced Cancer of the cervix. One of the most important complications of pelvic irradiation is radiation enteritis manifesting as an early effect and late effect. Advancement in radiotherapy has brought about tremendous improvement in target volume conformity using techniques such as Intensity Modulated Radiotherapy and the use of PROTON therapy. Due to limited access to these innovations many centers, including Ocean Road Cancer Institute, are not able to employ these newer techniques. As a result, there lies a challenge in minimizing exposure to the organs at risk. While the use of bladder protocol enhances reproducibility in EBRT during cervical cancer treatment, it also plays a vital role in pushing the bowel bag out of the radiation field. In Ocean Road Cancer Institute, Bladder protocol is a component of the daily treatment procedure for cervical cancer radiotherapy. However, there is a paucity of data on how well patients can comply with bladder instructions from simulation to the 25^{th} session of treatment. With a majority of patients reporting enteritis-related complaints during treatment, it is important to determine the bladder protocol compliance pattern and its relation with grades of enteritis across all weeks of External Beam Radiotherapy.

Objective: To assess bladder protocol compliance and its effect on the development of radiation enteritis among cervical cancer patients treated with radiotherapy at Ocean Road Cancer Institute.

Materials and Methods: This was a single hospital-based prospective cohort study, conducted entirely in Ocean Road Cancer Institute from October 2022 to April 2023. The study population consisted of histologically confirmed cervical cancer patients receiving Teletherapy during the stipulated period and meeting the eligibility criteria. A total of 79 patients were recruited and followed from baseline to their last week of external beam radiotherapy. Endpoint was the weekly highest grade of enteritis. Bladder volume estimation by urine volume was used to check for compliance whereas, Common Terminology Criteria for Adverse Events scale was used to grade enteritis. Statistical Package for Social Science was used for analysis. Quantitative data

were summarized using mean, standard deviation, and percentages. Comparison between bladder volumes from baseline to the last week of treatment was obtained using Analysis of Variance (ANOVA) for repetitive variables. Correlation between weekly bladder protocol compliance and weekly grade of enteritis was obtained using Spearman's correlation method whereas the significance in the difference of proportion between different grades of enteritis weekly was obtained using CHI square test. P-value of <0.05 was considered statistically significant.

Results: The mean urine volume at simulation was 296(± 190 SD) while at week 5 the mean urine volume was 231.2 (± 162 SD) which represented a 21.9% drop from baseline with a P-value of 0.003. There was an increment in mean bladder volume by 4% and 1% in weeks 1 and 2 respectively with p-values of 0.201 and 0.745 respectively. In weeks 3 and 4, the mean urine volume dropped by 12.7% and 15.3% respectively, with p-values of 0.011 and 0.009 respectively.

The highest grade enteritis was grade I(5%), III(1%), III(4%), III(16%) and III(4%) in weeks 1,2,3,4 and 5 respectively with p-value of <0.001. correlation between mean weekly urine volume and grade enteritis yielded an inverse relationship with increasing strength of association towards week 5 and a p-value of 0.001 from weeks 2-5.

Conclusion: Patients are less compliant with bladder protocol toward the last weeks of external beam radiotherapy. These could be due to dose-related toxicity such as radiation-induced cystitis or inadequate reinforcement of the bladder protocol practice. More severe forms of radiation-induced enteritis are relatively higher in the last three weeks of treatment. Poor bladder protocol compliance in weeks 3-5 is associated with increased grade 2 and 3 enteritis in the respective weeks of treatment.

LIST OF ABBREVIATIONS

3D-CFRT Three-dimension conformal radiotherapy

ANOVA Analysis of variance

BMI Body mass index

BT Brachytherapy

CHT Chemotherapy

CT Computed tomography

EBRT External beam radiotherapy

IMRT Intensity modulated radiotherapy

IRB Institutional review board

MUHAS Muhimbili University of Health and allied sciences

ORCI Ocean road cancer institute

RF Renal failure

RT Radiotherapy

SD Standard deviation

TAH Transabdominal hysterectomy

DEFINITION OF KEY TERMS

Radiotherapy: Treatment modality involving the use of X-rays or other forms of radiation.

Teletherapy: radiotherapy technique whereby the treatment target is placed at some distance from the source of radiation

Brachytherapy: Technique involving the placement of radiation source in close contact with the target tissue.

Bladder protocol: It is a system of rules or instructions that require a comfortably full bladder during pelvic irradiation to limit the exposure of the small bowel to ionizing radiation.

Compliance: The state of obeying or being in accordance with established guidelines or specifications.

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CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

Cervical cancer is the most common malignancy in Tanzania accounting for 25% of all cancer incidence(1). In females, it accounts for 40.7% of all cancer incidence nationwide(1). These statistics are accompanied by an age-standardized mortality burden of 42.7 deaths per 100000(2).

Currently, radiotherapy remains a vital modality in the overall management of cancer for both curative and palliative intents of care. An estimated 50% of all cancer patients receive radiotherapy during their course of treatment and this accounts for an approximately 40% component of curative treatment(3). Despite its impressive impact on tumor control, Irradiation can also cause adverse effects on the surrounding normal tissues which may manifest acutely or at a delayed time from actual radiotherapy treatment. In the management of Uterine Cervix Carcinoma, radiotherapy is indicated as the primary treatment for locally advanced disease (FIGO 2018 stage IB3, IIB-IVA) (4).

Definitive Radiotherapy for cervical cancer involves Teletherapy (EBRT) and Brachytherapy (BT) components, and both possess significant potential for serious radiotherapy induced side effects on normal tissues. EBRT to the pelvis during treatment not only delivers radiation to the target volume but also to the nearby structures covered in the beam field especially when using techniques with low target volume conformity(5)(3)(6)(7)(8). One of the most common toxicities encountered is the development of radiation enteritis as a result of irradiation of the bowel(9)(10). Historically, various technological advancement, such as the introduction of 3DCFRT, IMRT, and PROTON therapy, have enabled the improvement of target volume versus beam coverage conformity(6). In resource limited settings, realization of this improvement is hampered by scarcity. Other techniques have also been recommended which include treatment in prone position with belly board as well as utilization of bladder protocol in supine position(11).

Despite the above improvements, Radiation enteritis-related symptoms are part of the main complains reported by patients during weekly review of cervical cancer treatment related toxicity. Radiation enteritis occurs in majority of patients during treatment(12). Symptoms range from mild; nausea, vomiting, anorexia, diarrhea and abdominal discomfort, to severe forms requiring intensive in-hospital management, and may lead to interruptions of treatment(10)(9).

Bladder protocol intervention utilizes the anatomic variation that occurs with respect to the position of the lower part of the small bowels as function of bladder volume. It involves a set of instructions to the patients with the aim of having a comfortably full bladder during treatment simulation as well as during actual treatment. In most institutions, patients are required to void then take 300-500mls of water and wait for 30 minutes before treatment session. It is most useful during supine treatment position for pelvic irradiation.

As the patient progress through the treatment period a number of side effects usually develop, which include bladder irritation due to inflammatory reaction triggered by radiation injury(13). With the bothersome symptoms of acute cystitis such as urgency, dysuria and frequency it is possible that patients may end up being non-compliant to bladder protocol and this might contribute to an increased severity of radiation enteritis both acute and delayed forms.

A number of studies have looked at the maintenance of constant bladder volume during pelvic irradiation as well as the accompanying geometrical alteration in rectal, prostate and cervical cancer patients(14)(15)(16)(17). The role of full bladder volume in minimizing radiation enteritis has well been established, however, limited data exists on how well patients are able to comply with the protocol thus creating a need for a further inquiry into this practice.

1.2 Problem Statement

At ORCI, bladder protocol is a major intervention employed to limit bowel exposure to irradiation during EBRT treatment of cervical cancer with the aim of reducing the severity and incidence of radiation enteritis. However, a majority of patients develop enteritis during the course of treatment with more severe grades towards the last week of therapy. It is still not yet established if this phenomenon is due to poor compliance.

In addition, there exist a knowledge gap on how well patients are able to comply with the bladder protocol instruction from the time of simulation to the last session of EBRT, and its ultimate influence on their predisposition to developing radiation enteritis.

Thus, there is a need to have a data supported judgement on the effectiveness of this practice in order to facilitate improvement of compliance.

1.3 Conceptual framework

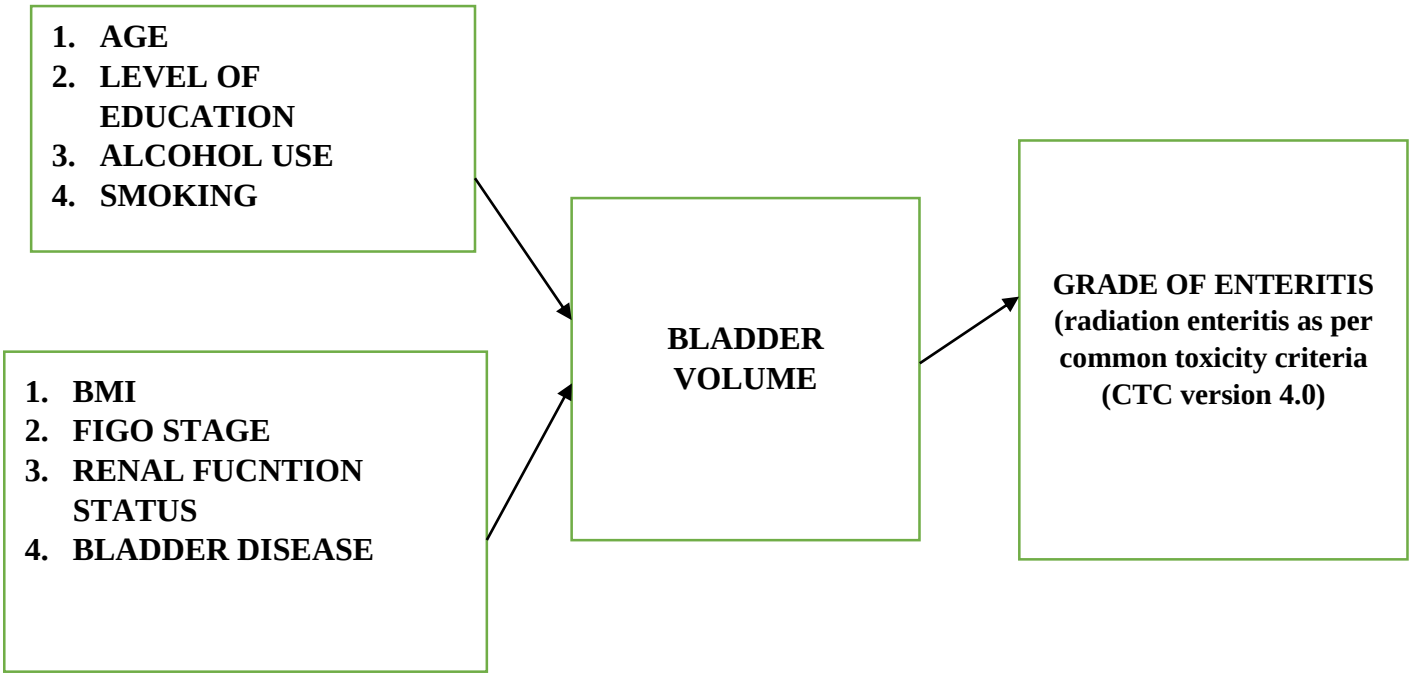


Figure 1: Sequential relationship

diagram depicting the interaction between independent and dependent variables:-increased age is associated with decreased bladder volume; level of education will influence the degree of adherence to bladder filling instruction; smoking and alcohol consumption can potentiate kidney impairment causing impaired bladder filling; low BMI, advanced stage, impaired renal function and bladder diseases are all associated with decreased bladder volume; Low bladder volume during irradiation can potentially lead to higher grade enteritis

1.4 Rationale

Findings from this study can provide the knowledge on the overall bladder protocol compliance at Ocean Road and further inform guideline adjustment in improving compliance as well as initiate further probe into possible causes of non-compliance.

Assessment of the relationship between weekly compliance and grade enteritis can bridge the knowledge gap on whether radiation induced enteritis observed among patients at ocean road is due to non-compliance

1.5 Research questions

From the general inference statement that, 'bladder protocol should be observed during each session in order to minimize the volume of bowel exposure to irradiation', the following were the research questions; -

1.5.1 Overall research question

- How is bladder protocol compliance and its effect on radiation enteritis among cervical cancer patients at Ocean Road Cancer Institute?

1.5.2 Specific research questions

1. Are patients complying with the bladder protocol requirement throughout treatment period at ORCI?
2. Which of the 5 weeks of EBRT have the least bladder protocol compliance among cervical cancer patients treated with radiotherapy at ORCI?
3. Which of the 5 weeks of EBRT have the highest rate of grade 2 and 3 enteritis among cervical cancer patients treated with radiotherapy at ORCI?

4. What is the relationship between weekly compliance and grade of enteritis among cervical cancer patients treated with radiotherapy at ORCI?

1.6 Broad objective

To assess bladder protocol compliance and its effect on radiation enteritis among cervical cancer patients at Ocean Road Cancer Institute from Nov 2022 to Jan 2023

1.7 Specific objectives

1. To assess bladder protocol compliance among cervical cancer patients on external beam radiotherapy at ORCI from Nov 2022 to April 2023
2. To determine which of the 5 weeks of EBRT have the least bladder protocol compliance among cervical cancer patients treated with radiotherapy at ORCI from Nov 2022 to April 2023
3. To determine which of the 5 weeks of EBRT have the highest rate of grade 2 and 3 enteritis among cervical cancer patients treated with radiotherapy at ORCI from Nov 2022 to April 2023
4. To assess the relationship between weekly compliance and grade of enteritis among cervical cancer patients treated with radiotherapy at ORCI from Nov 2022 to April 2023

1.8 Hypothesis

1.8.1 Null hypothesis

Bladder protocol compliance is the same from simulation to the last week of treatment and is not associated with increased grade of enteritis among cervical cancer patients at ORCI

1.8.2 Alternative hypothesis

Bladder protocol compliance is not the same from simulation to the last week of treatment and is associated with increased grade of enteritis among cervical cancer patients at ORCI

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Overview

2.1.1 Overall and weekly bladder protocol compliance during treatment

Maintaining a reproducible constant bladder volume from treatment planning to the entire treatment period has been a common challenge basing on various research findings globally(18). Various methods have been employed in monitoring bladder volume and bladder protocol compliance such as the use of CT scans, ultrasound scans, calculated estimates as well as urine collection in calibrated containers (17)(18)(16). In all occasions the findings from these methods have documented varying extent of mean bladder volume measurement deviation during treatment with reference to the mean value during simulation and planning (20)(16)(18)(21). These inconsistencies in the bladder volume as a result have a negative influence on the accuracy of irradiation field target volume and thus can result in volumetric and dosage alteration involving nearby normal tissues such as the small bowel(22). There is limited data about bladder protocol reproducibility in Africa and Tanzania during radiation treatment among cervical cancer patients.

2.1.2 Occurrence of enteritis RTOG grade during treatment

Radiation-induced intestinal injury manifests acutely during the treatment period with a varying spectrum of clinical signs and symptoms that can be mild, moderate or severe depending on the RTOG severity grading scale(23). Mild features are usually self-limiting while moderate to severe forms accompany a significant morbidity with detrimental effects on quality of life as well as overall performance status(23). During five weeks of treatment time, the occurrence of features due to enteritis displays a weekly pattern characterised by lesser high-grade enteritis during the early weeks of treatment as compared to later weeks (17).

2.1.3 Relationship between bladder volume and radiation enteritis in managing cervical cancer.

The importance of bladder volume in determining small bowel involvement in the radiation field during pelvic teletherapy has already been established. Empty bladder is associated with more bowel toxicity in terms of both grade and frequency whereas full bladder confer more protection by pushing the some volume of the bowel off the radiation field (24). Many other techniques such as prone position using bellyboard have been employed but supine position with comfortably full bladder has proven to be superior(11). Other factors such as concurrent chemotherapy, hypertension, diabetes, inflammatory bowel disease and immune status have also been linked with increased risk of radiation enteritis, however, bladder volume during pelvic irradiation has been proven to be an independent risk factor(8)(25)(26)(27)(10).

CHAPTER THREE

3.0 STUDY METHODOLOGY

3.1 Study setting

This study was conducted entirely at Ocean Road Cancer Institute for six months. ORCI is a cancer referral facility located along Barack Obama Road in Dar es Salaam. It is one of the oldest health facilities having founded in 1895. It is also Tanzania's largest cancer facility and currently carries out the majority of cancer treatment nationwide.

3.2 Study type and design

This was a prospective cohort type covering newly diagnosed cervical cancer patients followed through their respective course of external beam radiotherapy.

3.3 Study population

This study covered a population composed of newly diagnosed cervical cancer patients planned for/receiving curative EBRT at ocean road cancer institute from 1st November 2022 to 31st April 2023

3.4 Sample size calculation

Sample size calculation was done Using Kish Leslie's formula. The primary endpoint being radiation enteritis, a proportion of 90% prevalence of radiation induced enteritis (12) was used with a 95% confidence interval and a margin of error (Ɛ) of 0.07 plus a non-response rate of 10%

Z = z-score

P = proportion

n0 = sample size

n0 = Z2P (1-P)/Ɛ*2

1.962x0.9 (1-0.9) /0.07*2= 71 including non-response 10% then= 71/0.9 = **79 cervical cancer patients**

3.5 Selection

Eligibility

1. **Inclusion criteria** -All patients with histologically confirmed invasive squamous cell carcinoma of the cervix stage 1b3- 4A that were planned for curative EBRT during the study period
2. **Exclusion criteria** - Patients with bladder incontinence or leakage due to any reason, patients with bladder outlet obstruction, patients with bladder filling impairment.

3.6 Sampling strategy

Sampling relied on the simulation appointment list where all patients planned for EBRT were recorded. All patients meeting the inclusion criteria were approached for consenting during their date of appointment and prior to simulation.

3.7 Measurements

Compliance: The reference point was defined by the mean bladder volume at simulation (100%). This was then compared by the respective weekly mean bladder volume during actual treatment to establish variation.

Radiation enteritis: This was measured as grade 1,2 or 3 based on common terminology criteria for adverse events as follows:

Grade 1 (Mild)

Symptoms: Asymptomatic or mild symptoms.

Impact: Minimal; no significant impact on daily activities.

Intervention: No intervention required or symptomatic treatment only.

Grade 2 (Moderate)

Symptoms: Moderate symptoms such as diarrhea (requiring ≤4 stools/day over baseline) or abdominal pain.

Impact: Some interference with daily activities.

Intervention: Oral medications, dietary modifications, or other non-invasive treatments.

Grade 3 (Severe)

Symptoms: Severe symptoms such as diarrhea (≥7 stools/day over baseline), severe abdominal pain, or requiring intravenous fluids for dehydration.

Impact: Significant impact on daily activities; often requiring medical intervention.

Intervention: Hospitalization may be required for intravenous fluids, medications, or other intensive treatments.

Grade 4 (Life-threatening or Disabling)

Symptoms: Life-threatening symptoms like bowel obstruction, perforation, or hemorrhage.

Impact: Major impact on quality of life and daily function.

Intervention: Requires urgent operative intervention, intensive care, or other critical interventions

The percentage weekly distribution was obtained to established a severity pattern to be compared against compliance.

3.8 Data collection technique

Data collection employed the use of a structured tool as follow;

1. **Main questionnaire**

This was tailored to cover patients' demographics, respective variables both independent and dependent. (To be administered by the principal investigator). Contained enteritis grading scale and respective fields of entry which were scored weekly and recorded by the principal investigator.

2. **Urine collection chart**

A separate page in the main data collection tool with tabulation for the filling of post simulation and post treatment voided urine volumes in milliliter. This was administered by either research assistant or principal investigator.

3.9 Pre-testing

This was conducted two weeks prior to the commencement of the actual data collection, from 17th Nov 2022- 31st Nov 2022. Data collected at this phase was not be used for analysis.

3.10 Independent variables

1. Age
2. Level of education
3. Alcohol use
4. Smoking
5. BMI
6. Renal function status
7. Bladder disease
8. FIGO stage

3.11 Dependent variables;

1. Bladder volume
2. Grade of enteritis

3.12 Data Management

In order to ensure data reliability, identical calibrated containers were used for bladder volume estimation via collected urine. In addition to this, uniform data collection tool comprising of closed ended qualitative responses as well as uniform scale of measurement for BMI, urine volume and grade of enteritis was employed.

Accuracy of the collected data were ensured by use of the standardized scale of measurement for the respective variables. Grade enteritis was measured using CTCAE scale which is a uniform scale. From the findings that measurement of collected urine using calibrated containers is as useful as ultrasound estimation of bladder volume(17), bladder volume was estimated on milliliter scale using calibrated containers. The questionnaires were reviewed for completeness and accuracy before data entry.

3.13 Data analysis

Statistical Package for Social Science (SPSS v.25) was used for statistical analysis. Categorical variables were summarized using proportions and continuous variables were summarized using mean and standard deviation. Reference mean bladder volume w obtained by summation of all patients' urine volume at simulation and dividing the value by the total number of patients simulated. Comparison between the measurement of urine output from baseline to the last week of EBRT was obtained using Analysis of Variance (ANOVA) for repetitive variables.

Weekly incidence of grade 1,2 and 3 enteritis, respectively, was measured as a percentage of total number of patients followed for that week. Correlation between urine volume and grade of enteritis was obtained using spearman's correlation method. Significance in difference of proportion between different grades weekly was obtained using Chi square test. P value of less than 0.05 was considered statistically significant.

Compliance/bladder or urine volume variation	ANOVA
Weekly grade 1,2 and 3 distribution	Chi square test
Correlation between compliance and grade enteritis	Spearman's correlation method

3.14 Ethical issues

This study involved human subjects and the right to voluntary participation and privacy was of paramount importance. A written signed informed consent was used where information regarding any benefit, risk, confidentiality and contact information was disclosed prior to consenting. Patients voluntarily signed the written document at the end of consenting process by either rendering their signatures or thumb print.

Identity was limited to the subject's initials and respective study identity number throughout the study period.

Ethical clearance was sought from MUHAS IRB and permission to conduct this study was obtained from the Directorate of Research Ocean Road Cancer institute.

3.15 Study limitation and mitigation

Limitations:

Regular voiding into a calibrated container might have been quite an inconvenience to some patients

Mitigation:

In both cases proper counselling during recruitment was employed with emphasis on challenges and the need for readiness.

CHAPTER FOUR

4.0 RESULTS

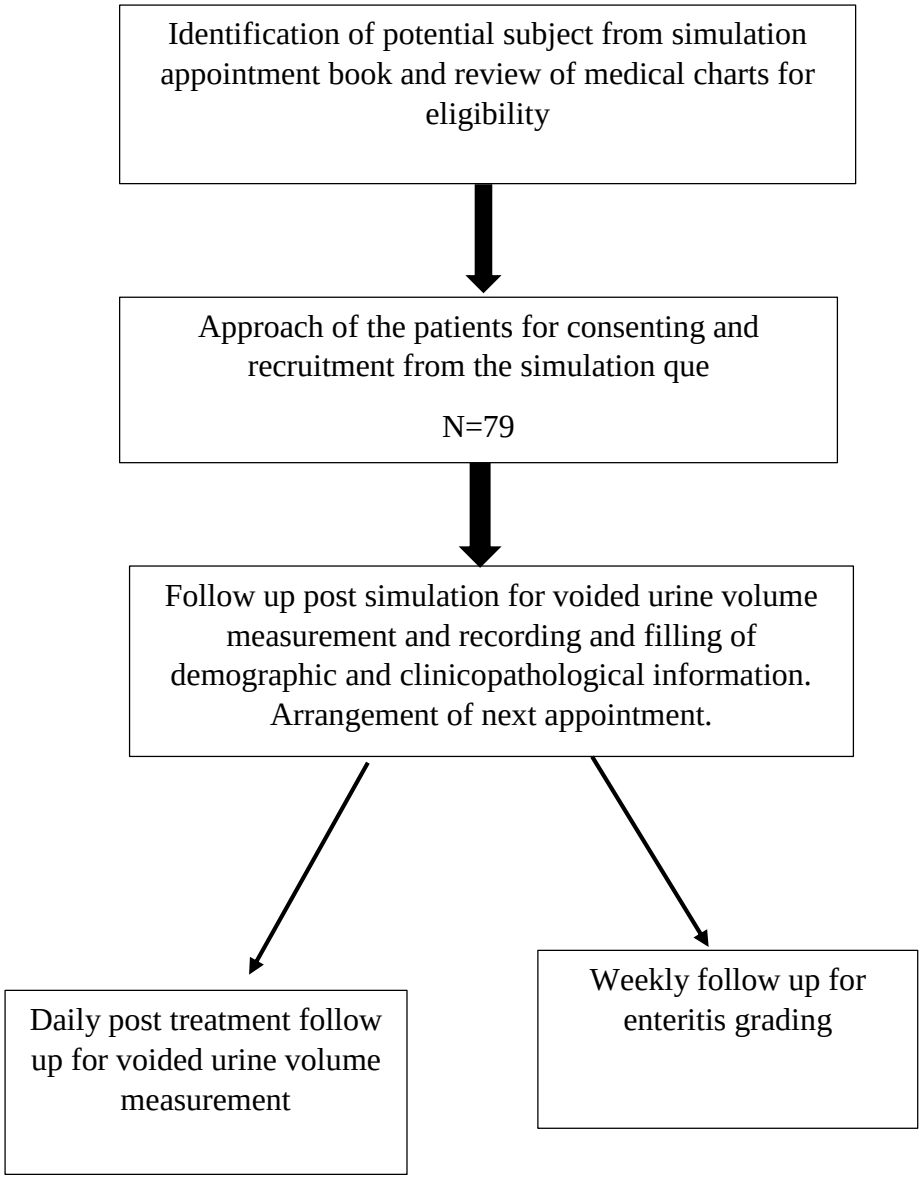


Figure 2: Flow chart to illustrate workflow

4.1 Patients' Characteristics

Sociodemographic characteristics

A total of 79 patients (N=79) were recruited in this study and followed from simulation to the last day of external beam radiotherapy. All patients were able to complete their planned five weeks of EBRT without interruption. These comprised a total dose of 50 Gy in 25 fractions given five days per week. The mean age in years was 54(+/- 12SD) and the median age was 54 ranging from 26-78 years. In terms of age grouping, (40.5%) were < 50 years while (59.5%) were >50 years. On the assessment of education status; (48.1%) had no formal education, (45.6%) had only received primary education, (5.1%) had secondary education and (1.3%) had a university education. Among the 79 study participants, (94.94 %) reported no history of smoking and 70.89% reported no history of alcohol use. Table 1 summarizes the sociodemographic characteristics of the participants.

Table 1: Sociodemographic characteristics of the study participants N=79

Variables	Characteristics	Frequency	Percentage
Age	Mean(±SD)	54(±12)	
	Median(range)	54(26-78)	
Age Group	< 50	32	40.51
	>50	47	59.49
Education Level	None	38	48.10
	Primary	36	45.57
	Secondary	4	5.06
	University	1	1.27
Smoking	No	75	94.94
	Yes	4	5.06
Alcohol	No	56	70.89
	Yes	23	29.11

Clinicopathological characteristics

Patients were staged according to FIGO staging. (3.8%) had IB, (11.4%) IIA, (55.7%) IIB, (10.1%) IIIA and (19%) IIIB. Body mass index was graded according to the WHO scale; 45.6% had a healthy weight, 20.3% were heavy weight, 15.2% were Obese and 19% were underweight. 75.95% had normal renal function status based on measured creatinine level. Table 2 below summarizes the clinicopathological characteristics of the study participants.

Table 2: Clinicopathological characteristics of the study participants N=79

Figo Staging	IB	3	3.80
	IIA	9	11.39
	IIB	44	55.70
	IIIA	8	10.13
	IIIB	15	18.99
BMI	Health Weight	36	45.57
	Heavy Weight	16	20.25
	Obesity	12	15.19
	Underweight	15	18.99
RFT	Normal	60	75.95
	Impaired	19	24.05

4.2 Urine Volume Measurement and Compliance

The mean urine volume at simulation was 296(+/-190SD), lowest 10mls and the highest 700mls. Weekly mean urine volume was 308(+/-182SD), 300(+/-180SD), 258.5(+/-161SD), 250.7(+/-168SD) and 231.2(+/-162SD) for weeks 1,2,3,4 and 5 respectively. These represented a (4%) and (1.4%) rise in mean urine volume from baseline for weeks 1 and 2 respectively. In weeks 3,4 and 5 there was a drop in mean urine volume by (12.7%), (15.3%) and (21.9%) respectively. Analysis of variance using ANOVA for repetitive measures yielded differences of -12,7, -3.4, 37.5, 45.3, and 64.8 with p-values of 0.201, 0.745, 0.011,0.009 and 0.003 for weeks 1,2,3,4 and 5 respectively. Table 3 summarizes results for urine volume measurement and compliance supported by graph 1 below.

Table 3: Summary of results for urine measurement and compliance

Action	Mean(±sd)	Difference	95% CI	P value
Simulation	296(±190)			
Week 1	308(182)	-12.7	-32, 6.9	0.201
Week 2	300(180)	-3.4	-24, 17.4	0.745
Week 3	258.5(161)	37.5	8.9 , 66.1	0.011
Week 4	250.7(168)	45.3	9.34, 76.4	0.009
Week 5	231.2(162)	64.8	15.3 , 114.4	0.003

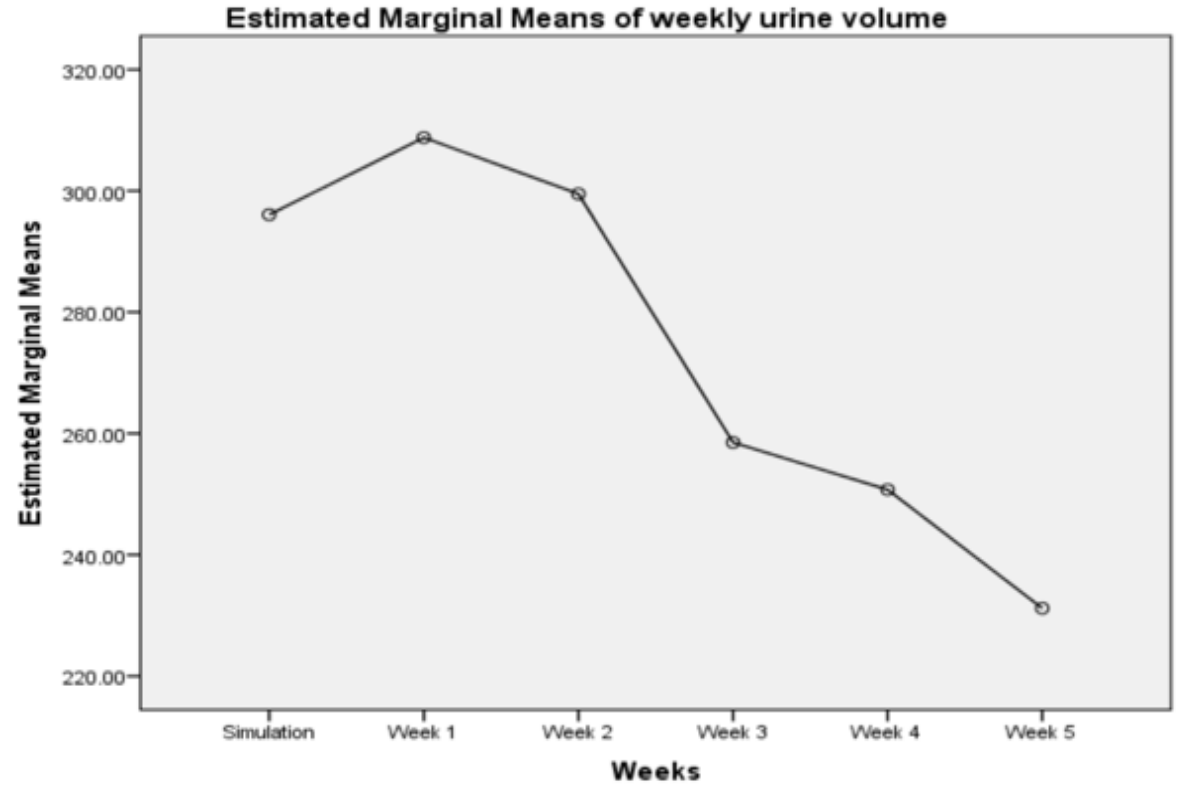


Figure 3: Depicting the variation of mean weekly bladder volume from the simulation baseline

The graph shows an initial rise in the mean urine volume in week 1, this is followed by a slight drop in week 2 but still remains above the baseline mean. There is a further steeper drop from 2 to week 3 progressing to the 5^{th} week.

4.3 Assessment of Enteritis

There were changes in the distribution of grade of enteritis from weeks 1 to 5. In week 1 the highest grade of enteritis was grade 1(5%) while in weeks 2-5, the highest grade was grade 3. There was an increase in proportion of grades 2 and 3 towards weeks 4 and 5. Week 4 had the highest proportion of grade 3(16%). Week 5 had the highest proportion of grade 2(48%). The difference between the distribution of grade enteritis between consecutive weeks yielded a p-value of <0.001 as obtained by the Chi square test. Bar chart 1 provides a summary of the distribution of grade enteritis across the 5 weeks of treatment

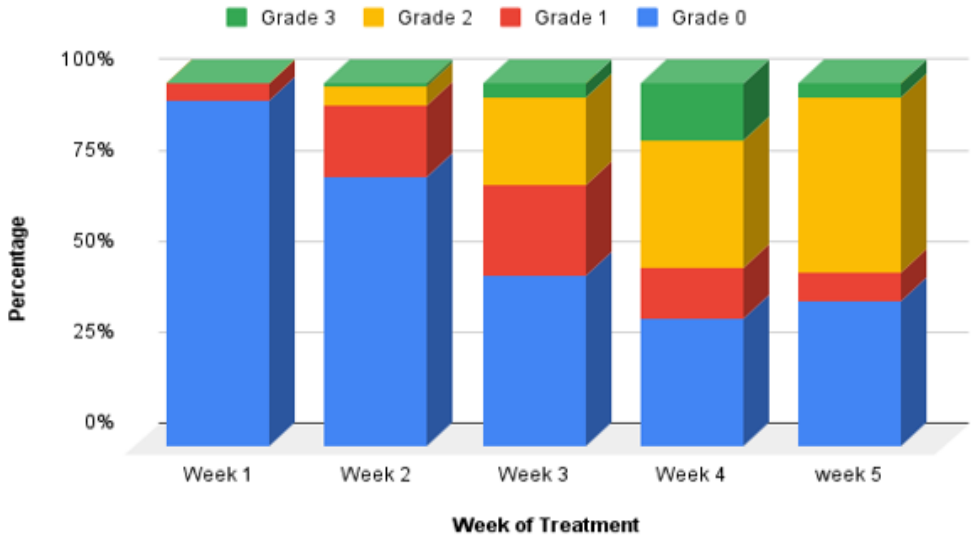


Figure 4: Show percentage distribution of various grades of enteritis across 5 weeks of EBRT

4.4 Correlation of Bladder Volume and Enteritis

The mean weekly bladder volumes were compared every week across the respective grades of enteritis and the results showed progressive decrement in mean from the 1st week of treatment to the last week. This was accompanied by an increment in grade 2 and 3 enteritis. The spearman correlation method yielded negative values for the coefficients as shown in Table 5 and the strength of correlation increased towards week 5. The correlation from weeks 2-5 was statistically significant.

Weekly mean volume vs weekly grade enteritis	SPEARMAN'S CORRELATION CO-EFFICIENT	p-value
Week 1	-0.19	0.08
Week 2	-0.34	0.001
Week 3	-0.51	0.001
Week 4	-0.55	0.001
Week 5	-0.61	0.001

CHAPTER FIVE

5.0 DISCUSSION

The results showed an increment in bladder volume, from the reference baseline mean, during the first and second weeks of treatment. However, the variation of the respective mean volumes was not statistical significance. This denotes some degree of compliance with bladder protocol during weeks 1 and 2. In weeks 3-5, there was a significant drop in mean weekly urine volumes culminating in (21.9%) at week 5. These variations were statistically significant hence confirming that patients become less compliant with bladder protocol instructions as they progress toward the last weeks of treatment.

It is difficult to maintain a constant urine volume during the whole course of treatment(16), however standardized bladder protocol enhances uniformity(18)(14)(21). Despite these, various studies have reported a decreasing trend in inter-fraction bladder volume from simulation through to the end of pelvic EBRT (16,17,21). In a study by Ahmad et al, on inter-fraction variability of bladder filling, a (78%) reduction in mean bladder volume was found at week 6 during EBRT for cervical cancer (28). In another study by Nakamura et al, there was a (38%) decrease in, mean bladder volume from baseline, by week 6 of EBRT while Sweta et al reported a (21%) drop in mean bladder volume at week 6(29)(17). These may be explained by diminished re-enforcement of bladder protocol requirements to patients. O' Doherty et al. demonstrated the role of labor-intensive repetitive implementation of pre-treatment preparations, such as bladder protocol in improving compliance(30). Progression into treatment may also result in dose-related cystitis which can impact bladder protocol compliance as a result of its bothersome symptoms of urgency, bladder discomfort, and frequency(13)(31). In addition, as treatment progresses, other multi-systemic side effects such as dehydration and anorexia might set in and consequently reduce fluid output(31).

Development and severity of radiation enteritis during pelvic irradiation are influenced by the volume of bowel bag present in the irradiated volume as well as the cumulative dose(8). As treatment time progress from week 1 to 5, more fractions of the prescribed dose are delivered thereby increasing the probability of adverse effects. This phenomenon could have led to the

increment in the proportion of grade 2 and 3 enteritis witnessed in this study. By comparing the 5 weeks, week 4 had the highest percentage of grade 3(16%) than week 5. Early intervention at grade 2 enteritis during week 4 could have prevented the development of more severe grade 3 enteritis in week 5

Bladder volume influences both the volume of the bowel bag in the irradiation field as well as enhances reproducibility of the target position(21)(14). In this study, there was an observed decrease in mean bladder volume as treatment advanced towards the last weeks while grade 2 and 3 enteritis increased. Analysis of the correlation between these variables using the spearman method showed a negative relation with statistically significant correlation coefficients from weeks 2-5. There was also an increment in the strength of correlation as weeks of treatment advanced towards week 5. This signifies the role of low bladder volume in increasing the probability of the increase in the severity of radiation enteritis. Several other factors have also been suggested as having the potential to influence enteritis(8)(9)(5)(11)(12). These factors include; HIV status, Diabetic, and concurrent cisplatin as well as autoimmune disease such as inflammatory bowel disease (5)(19)(8)(12)(25)(26). However, in a study by Quan Li et al on the dose-volume effect of acute diarrhea, the volume of irradiated small bowel was found to be an independent risk factor for the development of enteritis in all patients regardless of the other clinicopathological factors(8). Since full bladder reduces the volume of small bowel in the irradiation field by superior displacement, the decrease in the mean bladder volume in weeks 3-5 means that more volume of small bowel will be irradiated and therefore more grade 2 and 3 enteritis(14)(17). This has further been demonstrated by Nijkamp et al where an increase in bladder volume by 100 cc led to a V15 reduction of (16%)(32).

CHAPTER SIX

6.0 STUDY LIMITATIONS, CONCLUSIONS AND RECOMMENDATIONS

6.1 Study Limitation

- Assessment of bladder volume using a calibrated container is cumbersome and not easy to follow a larger sample
- Urine collection relied on patients' cooperation and could not account for spillage.

6.2 Conclusion

Bladder protocol compliance is significantly reduced as the patient edge towards the end of EBRT at Ocean Road Cancer Institute. There is also an increase in grades 2 and 3 as treatment progresses towards weeks 4 and 5. A significant association exists between bladder protocol compliance and the severity of enteritis.

More efforts should be put in place to ensure bladder protocol instructions are followed throughout the course of treatment as well as explore other possible factors leading to non-compliance. Other Radiation-induced side effects such as cystitis should be addressed both prophylactically and timely upon onset

6.3 Recommendations

- Patients should be made aware of the advantage of the various pre-treatment preparation rather than just mere instructions.
- Patients should be reminded repeatedly and regularly about the bladder protocol and other preparations

REFERENCES

1. Republic U. Globocan 20202 Tanzania. Popul Policy Compend. 2020;1–6.
2. World Health Organization. Costing the National Response to Cervical Cancer : United Republic of Tanzania , 2020 – 2024. Who. 2020;(November):2020–4.
3. Baskar R, Lee KA, Yeo R, Yeoh KW. Cancer and radiation therapy: Current advances and future directions. Int J Med Sci. 2012;9(3):193–9.
4. United THE, Of R, Health MOF, Development C. National-Cancer-Treatment-Guidelines2.pdf. Available from: http://kehpca.org/wp-content/uploads/National-Cancer-Treatment-Guidelines2.pdf
5. Loge L, Florescu C, Alves A, Menahem B. Radiation enteritis: Diagnostic and therapeutic issues. J Visc Surg [Internet]. 2020;157(6):475–85. Available from: https://doi.org/10.1016/j.jviscsurg.2020.08.012
6. Meyer J, Czito B, Yin F-F, Willett C. Advanced radiation therapy technologies in the treatment of rectal and anal cancer: intensity-modulated photon therapy and proton therapy. Clin Colorectal Cancer. 2007 Jan;6(5):348–56.
7. Andreyev HJN, Wotherspoon A, Denham JW, Hauer-Jensen M. "Pelvic radiation disease": New understanding and new solutions for a new disease in the era of cancer survivorship. Scand J Gastroenterol [Internet]. 2011 Apr 1;46(4):389–97. Available from: https://doi.org/10.3109/00365521.2010.545832
8. Li Q, Chen J, Zhu B, Jiang M, Liu W, Lu E, et al. Dose Volume Effect of Acute Diarrhea in Post-Operative Radiation for Gynecologic Cancer. Rev Investig Clin organo del Hosp Enfermedades la Nutr. 2017;69(6):329–35.
9. Hauer-Jensen M, Denham JW, Andreyev HJN. Radiation enteropathy--pathogenesis, treatment and prevention. Nat Rev Gastroenterol Hepatol. 2014 Aug;11(8):470–9.
10. Willett CG, Ooi C-J, Zietman AL, Menon V, Goldberg S, Sands BE, et al. Acute and late

toxicity of patients with inflammatory bowel disease undergoing irradiation for abdominal and pelvic neoplasms. Int J Radiat Oncol Biol Phys [Internet]. 2000 Mar 1;46(4):995–8. Available from: https://doi.org/10.1016/S0360-3016(99)00374-0

11. Kim TH, Kim DY, Cho KH, Kim YH, Jung KH, Ahn J-B, et al. Comparative analysis of the effects of belly board and bladder distension in postoperative radiotherapy of rectal cancer patients. Strahlentherapie und Onkol Organ der Dtsch Rontgengesellschaft . [et al]. 2005 Sep;181(9):601–5.

12. Stacey R, Green JT. Radiation-induced small bowel disease: latest developments and clinical guidance. Ther Adv Chronic Dis. 2014 Jan;5(1):15–29.

13. Browne C, Davis NF, Mac Craith E, Lennon GM, Mulvin DW, Quinlan DM, et al. A Narrative Review on the Pathophysiology and Management for Radiation Cystitis. Adv Urol. 2015;2015:346812.

14. Mullaney LM, O'Shea E, Dunne MT, Finn MA, Thirion PG, Cleary LA, et al. A randomized trial comparing bladder volume consistency during fractionated prostate radiation therapy. Pract Radiat Oncol. 2014;4(5):e203–12.

15. Cramp L, Connors V, Wood M, Westhuyzen J, McKay M, Greenham S. Use of a prospective cohort study in the development of a bladder scanning protocol to assist in bladder filling consistency for prostate cancer patients receiving radiation therapy. J Med Radiat Sci. 2016 Sep;63(3):179–85.

16. Hynds S, McGarry CK, Mitchell DM, Early S, Shum L, Stewart DP, et al. Assessing the daily consistency of bladder filling using an ultrasonic Bladderscan device in men receiving radical conformal radiotherapy for prostate cancer. Br J Radiol. 2011 Sep;84(1005):813–8.

17. Bandanatham S, Manur J. Compliance with bladder protocol during concurrent chemoradiation for cancer of the cervix and its impact on enteritis : A prospective. 2018;3:69–74.

18. Nasser NJ, Fenig E, Klein J, Agbarya A. Maintaining consistent bladder filling during external beam radiotherapy for prostate cancer. Tech Innov patient Support Radiat Oncol. 2021 Mar;17:1–4.

19. Andreyev HJN, Vlavianos P, Blake P, Dearnaley D, Norman AR, Tait D. Gastrointestinal symptoms after pelvic radiotherapy: role for the gastroenterologist? Int J Radiat Oncol Biol Phys. 2005 Aug;62(5):1464–71.

20. Stam MR, van Lin ENJT, van der Vight LP, Kaanders JHAM, Visser AG. Bladder filling variation during radiation treatment of prostate cancer: can the use of a bladder ultrasound scanner and biofeedback optimize bladder filling? Int J Radiat Oncol Biol Phys. 2006 Jun;65(2):371–7.

21. Luo H, Jin F, Yang D, Wang Y, Li C, Guo M, et al. Interfractional variation in bladder volume and its impact on cervical cancer radiotherapy: Clinical significance of portable bladder scanner. Med Phys. 2016 Jul;43(7):4412.

22. Braide K, Kindblom J, Lindencrona U, Månsson M, Hugosson J. The value of a bladder-filling protocol for patients with prostate cancer who receive post-operative radiation: results from a prospective clinical trial. Acta Oncol. 2019 Apr;58(4):463–8.

23. Kouloulias VE, Kouvaris JR. Cytoprotective efficacy of amifostine against radiation-induced rectal toxicity: Objective and subjective grading scales for radiomucositis. Molecules. 2008;13(4):892–903.

24. Sukhaboon J, Shotelersuk K, Lertsanguansinchai P, Khorprasert C. Reducing radiation dose to pelvic small bowel in cervical cancer patients treated with Ir-192 intracavitary brachytherapy by using urinary bladder distension. J Med Assoc Thai. 2005 Sep;88 Suppl 4:S200-6.

25. Ozkan EE, Erdemoglu E, Raoufi J. Impact of Diabetes on Gastrointestinal and Urinary Toxicity after Radiotherapy for Gynecologic Malignancy. J Turkish Soc Obstet Gynecol. 2019;

26. Alashkham A, Paterson C, Hubbard S, Nabi G. What is the impact of diabetes mellitus on radiation induced acute proctitis after radical radiotherapy for adenocarcinoma prostate? A prospective longitudinal study. Clin Transl Radiat Oncol. 2019 Jan;14:59–63.

27. Gichangi P, Bwayo J, Estambale B, Rogo K, Njuguna E, Ojwang S, et al. HIV impact on acute morbidity and pelvic tumor control following radiotherapy for cervical cancer. Gynecol Oncol [Internet]. 2006 Feb 1;100(2):405–11. Available from: https://doi.org/10.1016/j.ygyno.2005.10.006

28. Ahmad R, Hoogeman MS, Quint S, Mens JW, de Pree I, Heijmen BJM. Inter-fraction bladder filling variations and time trends for cervical cancer patients assessed with a portable 3-dimensional ultrasound bladder scanner. Radiother Oncol J Eur Soc Ther Radiol Oncol. 2008 Nov;89(2):172–9.

29. Nakamura N, Shikama N, Takahashi O, Ito M, Hashimoto M, Uematsu M, et al. Variability in bladder volumes of full bladders in definitive radiotherapy for cases of localized prostate cancer. Strahlentherapie und Onkol Organ der Dtsch Rontgengesellschaft . [et al]. 2010 Nov;186(11):637–42.

30. O'Doherty UM, McNair HA, Norman AR, Miles E, Hooper S, Davies M, et al. Variability of bladder filling in patients receiving radical radiotherapy to the prostate. Radiother Oncol J Eur Soc Ther Radiol Oncol. 2006 Jun;79(3):335–40.

31. Hall EJ. Radiobiology for the radiologist [Internet]. Hagerstown, Md. : Medical Dept., Harper & Row, [1973] ©1973; Available from: https://search.library.wisc.edu/catalog/999539825402121

32. Nijkamp J, Doodeman B, Marijnen C, Vincent A, van Vliet-Vroegindeweij C. Bowel exposure in rectal cancer IMRT using prone, supine, or a belly board. Radiother Oncol J Eur Soc Ther Radiol Oncol. 2012 Jan;102(1):22–9.

APPENDICES

Appendix I: Data collection tool

Serial number: **Date of recruitment:**

DEMOGRAPHIC INFORMATION

Patient's Initials:

Age:

Address:

EDUCATION

a) Primary
b) Secondary
c) University
d) None

HISTORY OF SMOKING

a) Negative
b) Positive

ALCOHOL CONSUMPTION

a) Negative
b) Positive

CLINICO-PATHOLOGICAL INFORMATION

INDICATE DISEASE STAGE:

BMI: _____.

RENAL FUNCTION STATUS

a) NORMAL (creatinine level 60-104 umol/L)
b) IMPAIRED (above 104 umol/L)

ANY MEDICAL HISTORY OF BLADDER DISEASE

a) NO
b) YES
c) SCHISTOSOMIASIS

IF YES SPECIFY:

WEEKLY RTOG GRADE ENTERITIS SCORE

	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
WHO Toxicity Grade	None	Increase of 2–3 stools per d over pretreatment	Increase of 4– 6 stools per d, or nocturnal stools, or moderate cramping	Increase of 7–9 stools per d, or incontinence, or severe cramping	Increase of >10 stools per d or grossly bloody diarrhea, or need for parenteral support
EORTC-RTOG scale for lower gastro-intestinal toxicity	None	Increased frequency or change in quality of bowel habits not requiring medication, rectal discomfort not requiring analgesics	Diarrhea requiring parasympatholytic drugs, mucous discharge not necessitating sanitary pads, rectal or abdominal pain requiring analgesics	Diarrhea requiring parenteral support, severe mucous or blood discharge necessitating sanitary pads/abdominal distension (flat plate radiograph demonstrates distended bowel loops)	Acute or subacute obstruction, fistula or perforation; gastrointestinal bleeding requiring transfusion; abdominal pain or tenesmus requiring tube decompression or bowel diversion

EORTC-RTOG= European Organization for Research and Treatment of Cancer/Radiation Therapy Oncology Group; WHO=World Health Organization.

1.1 RTOG GRADE ENTERITIS SCALE(23)

WEEK 1	WEEK 2	WEEK 3	WEEK 4	WEEK 5

VOIDED URINE VOLUME

TIME	@ CT-SIM	RT1	RT2	RT3	RT4	RT5	RT6	RT7	RT8	RT9	RT10	RT11	RT12	RT13	RT14	RT15	RT16	RT17	RT18	RT19	RT20	RT21	RT22	RT23	RT24	RT25
VOLUME (Mls)																										

Appendix II: Consent Form – English Version

Serial Number……..

CONSENT FORM.

Introduction

My name is Dr Mwitasrobert Gisiri, I'm a resident at the Muhimbili University of Health and Allied Sciences, Dar es Salaam. I'm researching on the Bladder protocol compliance and its effect on radiation induced enteritis during cervical cancer treatment period at Ocean Road Cancer Institute. I am going to give you information and invite you to be part of this research. Before you decide, you can talk to anyone you feel comfortable with about the research.

Purpose of the research

The purpose of this research is to assess how well enough are cervical cancer patients able to comply with bladder protocol instructions and the importance of this practice in influencing the development radiation induced enteritis. Information from this study will help in pointing how effective this practice is as well as provide reference for further guideline improvement in ocean road cancer institute.

What does participation involve?

If you agree to participate in this study, you will be interviewed using a data collection tool during which your social demographic and clinicopathological information will be recorded. In addition to that, your weekly review findings on clinical features of enteritis as well as your voided urine volume after simulation and each radiotherapy session will be recorded. Your participation in this research is entirely voluntary and you are allowed to withdraw at anytime.

Privacy:

All information will be kept confidential and only the researcher plus one research assistant will access it, no names will be used but identification numbers only. Your identity shall not be disclosed to anyone.

Risks:

No risks is anticipated as a result of your participation

Gains:

Your participation in the study will enable us to understand the gaps in the implementation of bladder protocol as an intervention in minimizing bowel exposure during radiotherapy for cervical cancer treatment. This will help guide future guideline improvement.

Who to Contact if you have questions about this study?

In case of any information about your rights as a participant in this study, please contact:

DR. MWITASROBERT GISIRI

EMAIL: gcrmwit@gmail.com

CELL: 0719449135

DR. CHRISTINA V. MALICHEWE

EMAIL: Christinamalichewe@gmail.com

CELL: 0767504315

DR. SIKUDHANI MUYA

EMAIL: sarahtk77@gmail.com

CELL: 0768776402

Patient's declaration:

I ……. Having read and understood the above information pertaining to this study, I hereby agree to participate in this study

Signature:

Thumb print if not able to sign:



Appendix III: Consent Form – Swahili Version

Nambari ya ushiriki……..

CHUO KIKUU CHA AFYA CHA MUHIMBILI

FOMU YA RIDHA YA USHIRIKI KATIKA TAFITI.

Mwanzo

Kwa majina naitwa Dkt Mwitasrobert Gisiri, mimi ni mwanafunzi wa shahada ya uzamili katika chou kikuu cha muhimbili, Dar es salaam. Ninafanya utafiti kuchunguza jinsi ambavyo protokali ya kibofu inavyozingatiwa Pamoja na uhusiano wake kwenye matukio ya adhari za mionzi kwenye utumbo mpana. Protokali ya kibofu ni mbinu inayomtaka mgonjwa kuwa na ujazo wa kutosha wa kibofu pindi anapopata mionzi ili kuzuia uwepo wa utumbo mdogo kwenye njia ya mionzi. Mbinu hii hutumika kama moja wapo ya njia za kupunguza adhari za mionzi kwenye utumbo. Nitakupa Habari Zaidi kuhusiana na utafiti huu na vilvile kukualika kushiriki kwenye tafiti hii. Kabla ya kufanya maamuzi , unaruhusiwa kupata ushauri kutoka kwa mtu yeyote kuhusu jambo hili.

Lengo la utafiti huu

Lengo la utafiti huu ni kuchunguza ni kwa kiasi gani wagonjwa wa saratani ya shingo ya kizazi wanazingatia maelekezo ya protokali ya kibofu na umuhimu wake katika kupunguza visa vya tatizo la utumbo litokanalo na mionzi. Matokeo ya utafiti huu yatasaidia kuonesha kipimo cha ufanisi wa mbinu hii na vile vile kutumika kwenye maboresho ya muongozo wa matibabu katika hospitali ya ocean road.

Jinsi ya kushiriki

Katika kushiriki katika tafiti hii, Habari zako zitarekodiwa kwa kutumia kifaa cha kukusanya data na itajumuisha Habari binafsi na vipimo. Pia matokeo ya kila wiki ya matibabu pamoja na kiasi cha mkojo utakao kojoa baada ya mchoro na kila baada ya tiba ya miozi yatarekodiwa. Ushiriki wako katika tafiti hii ni kwa hiari na unaruhusiwa kusitisha ushiriki mda wowote.

Faragha

Habari zako zitatunzwa kwa usiri mkubwa na mtafiti na wasaidizi wawili ndo wataruhisiwa kuzifikia. Pia matumizi ya majina kamili hayataruhusiwa bali kila mshiriki atatambulika kwa namba ya ushiriki tu.

Madhara ya utafiti huu

Hakuna madhara yeyote yanayotegemewa kutokea kutokana na ushiriki huu

Manufaa ya utafiti huu

Ushiriki wako katika utafiti huu utachangia kwenye takwimu ya kipimo cha ufanisi wa mbinu ya protokali ya kibofu na vile vile kupata Habari ya Ushahidi itakayo tumika katika maboresho ya muongozo katika siku za usoni.

Niwasiliane na nani kuhusu utafiti huu ?

Kwa mawasiliano yeyote kuhusu utafiti huu, wafuatao watahusika:

Dkt. MWITASROBERT GISIRI

BARUA PEPE: gcrmwit@gmail.com

SIMU: 0719449135

Dkt. CHRISTINA V. MALICHEWE

BARUA PEPE: Christinamalichewe@gmail.com

SIMU: 0767504315

Dkt. SIKUDHANI MUYA

BARUA PEPE: sarahtk77@gmail.com

SIMU: 0768776402

KIPENGELE CHA RIDHAA:

Mimi……., baada ya kusoma na kuelewa maudhui husika, ninaridhia kushiriki katika utafiti huu

Sahii:

Dole gumba iwapo huwezi kutia sahii:



Appendix IV: Ethical Clearance

UNITED REPUBLIC OF TANZANIA

MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

OFFICE OF THE DIRECTOR - RESEARCH AND PUBLICATIONS

Ref. No.DA.282/298/01.C/1423 Date: 27/10/2022

MUHAS-REC-10-2022-1423

Mwitas Robert Gisiri,
MMed in Clinical Oncology,
School of Medicine,
MUHAS

RE: APPROVAL FOR ETHICAL CLEARANCE FOR A STUDY TITLED: BLADDER PROTOCOL COMPLIANCE AND ITS EFFECT ON ACUTE RADIATION ENTERITIS AMONG CERVICAL CANCER PATIENTS AT OCEAN ROAD CANCER INSTITUTE.

Reference is made to the above heading.

I am pleased to inform you that the Chairman has on behalf of the University Senate, approved ethical clearance of the above-mentioned study, on recommendations of the Senate Research and Publications Committee meeting accordance with MUHAS research policy and Tanzania regulations governing human and animal subjects research.

APPROVAL DATE: 27/10/2022

EXPIRATION DATE OF APPROVAL: 26/10/2023

STUDY DESCRIPTION:

Purpose:

The purpose of this observational cohort study is to assess bladder protocol compliance and its effect on the development of radiation enteritis among cervical cancer patients treated with EBRT at ORCI.

The approved protocol and procedures for this study is attached and stamped with this letter, and can be found in the link provided: https://irb.muhas.ac.tz/storage/Certificates/Certificate%20-%2014255.pdf and in the MUHAS archives.

9 United Nations Road; Upanga West; P.O. Box 65001, Dar Es Salaam: Tel. G/Line: +255-22-2150302/6; Ext. 1038; Direct Line:+255-22-2152489;Telefax:+255-22-2152489;E-mail:drp@muhas.ac.tz;Web:https://www.muhas.ac.tz

The PI is required to:

1. Submit bi-annual progress reports and final report upon completion of the study.
2. Report to the IRB any unanticipated problem involving risks to subjects or others including adverse events where applicable.
3. Apply for renewal of approval of ethical clearance one (1) month prior its expiration if the study is not completed at the end of this ethical approval. You may not continue with any research activity beyond the expiration date without the approval of the IRB. Failure to receive approval for continuation before the expiration date will result in automatic termination of the approval for this study on the expiration date.
4. Obtain IRB amendment (s) approval for any changes to any aspect of this study before they can be implemented.
5. Data security is ultimately the responsibility of the investigator.
6. Apply for and obtain data transfer agreement (DTA) from NIMR if data will be transferred to a foreign country.
7. Apply for and obtain material transfer agreement (MTA) from NIMR, if research materials (samples) will be shipped to a foreign country,
8. Any researcher, who contravenes or fail to comply with these conditions, shall be guilty of an offence and shall be liable on conviction to a fine as per NIMR Act No. 23 of 1979, PART III section 10 (2)
9. The PI is required to ensure that the findings of the study are disseminated to relevant stake holders.
10. PI is required to be versed with necessary laws and regulatory policies that govern research in Tanzania. Some guidance is available on our website https://drp.muhas.ac.tz/.

Muhimbili University of Health and Allied Sciences
DIRECTOR
Research & Publications
Box 65001

Prof. Bruno Sunguya
Chairman, MUHAS Research and Ethics Committee
Cc: Director of Postgraduate Studies

9 United Nations Road; Upanga West; P.O. Box 65001, Dar Es Salaam: Tel. G/Line: +255-22-2150302/6; Ext. 1038; Direct Line:+255-22-2152489;Telefax:+255-22-2152489;E-mail:drp@muhas.ac.tz;Web:https://www.muhas.ac.tz

Appendix V: Introduction letter

UNITED REPUBLIC OF TANZANIA
MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY
MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES
OFFICE OF THE DIRECTOR – POSTGRADUATE STUDIES

In reply quote;
Ref. No. HD/MUH/T.50/2020

02nd November, 2022

The Executive Director,
Ocean Road Cancer Institute,
P.O. Box 3592,
DAR ES SALAAM

Re: INTRODUCTION LETTER

The bearer of this letter is Mwitasrobert Gisiri, a student at Muhimbili University of Health and Allied Sciences (MUHAS) pursuing MMed. Clinical Oncology.

As part of his studies he intends to do a study titled: "***Bladder Protocol Compliance and Its Effect on Acute Radiation Enteritis Among Cervical Cancer Patients at Ocean Road Cancer Institute***"

The research has been approved by the Chairman of University Senate.

Kindly provide him the necessary assistance to facilitate the conduct of his research.

We thank you for your cooperation.

Ms. Victoria Mwanilwa
For: DIRECTOR, POSTGRADUATE STUDIES

c.c. Mwitasrobert Gisiri

9 United Nations Road; Upanga West; P.O. Box 65001, Dar Es Salaam: Tel. G/Line: +255-22-2150302/6; Ext. 1015; Direct Line:+255-22-2151378;Telefax:+255-22-2150465;E-mail:dpgs@muhas.ac.tz;Web:https://www.muhas.ac.tz

Appendix VI: Permission undertake study

UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

OCEAN ROAD CANCER INSTITUTE

ORCI OCEAN ROAD CANCER INSTITUTE

On Reply Please Quote:

Ref: 10/VOL.XXI/107-B **Date:** 15th November 2022

INSTITUTIONAL ACADEMICS, RESEARCH, PUBLICATIONS AND ETHICS COMMITTEE (IARPEC)

Mwitasrobert Gisiri,
Candidate: MMed Clinical Oncology
Muhimbili University of Health and Allied Sciences.

Re: Permission to undertake a study titled 'Bladder Protocol Compliance And Its Effect On Acute Radiation Enteritis Among Cervical Cancer Patients At Ocean Road Cancer Institute'

Reference is made to the above heading and to the letter of introduction from the Director, Postgraduate Studies (MUHAS) dated 2nd November 2022 (Ref No. HD/MUH/T.316/2020) requesting for support to conduct this research at the Institute. It is noted that the study has already been approved by the Chairman of University Senate, MUHAS.

This is to inform you that the Institutional Academics, Research, Publications and Ethics Committee has granted you permission for the implementation of the above-mentioned study at ORCI for a period of one year from the date of this letter.

Upon successful completion of the study, you are obliged to submit a copy of the final document of this research project to the IARPEC.

OCEAN ROAD CANCER INSTITUTE ACADEMIC UNIT P.O. Box 3592 DAR ES SALAAM

Dr Nazima Dharsee MD, MMed, MSc
Director- Academic, Research and Consultancy Unit