RADIATION SIDE EFFECTS AND DETERMINANTS OF HEAD AND NECK CANCERS AT ORCI, DAR ES SALAAM, TANZANIA

Caroline Mrema, MD

Mmed (Clinical Oncology) Dissertation

Muhimbili University of Health and Allied Sciences

October , 2013

RADIATION SIDE EFFECTS AND DETERMINANTS OF HEAD AND NECK CANCERS AT ORCI, DAR ES SALAAM, TANZANIA

By

Caroline Mrema,MD

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

Muhimbili University of Health and Allied Sciences

October , 2013

CERTIFICATION

The undersigned certify that he has read and hereby recommend for acceptance the dissertation entitled "***Radiation side effects and Determinants in Head and Neck Cancers at Ocean Road Cancer Institute*"** in fulfillment of the requirements for the degree of Master of Medicine (Clinical Oncology) of Muhimbili University of Health and Allied Sciences.

_____

Dr. Khamza Maunda

(Supervisor)

_____

Date

DECLARATION

AND

COPYRIGHT

I, **Caroline Mrema**, declare that this **dissertation** entitled "***Radiation side effects and Determinants in Head and Neck Cancer at Ocean Road Cancer Institute***" is my own 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**_____

ABSTRACT

The vast majority of HNC are squamous cell carcinoma . Throughout the past two decades the efforts to improve the efficacy of treatment for locally advanced HNSCC have led to increased use of multimodality approaches combining surgery, radiotherapy , and chemotherapy

Most studies use chemotherapy as a treatment modality for HNSCC fail to stratify age in looking at outcome. Currently, available studies looking at outcomes with regards to patient age give little to no data about specific chemotherapeutic agents or radiation techniques and dosing. Given that less than 2% of HNSCC patients are enrolled in clinical trials worldwide, only future enrollment of all patients into clinical trials can give us knowledge about the role of treatment modality and outcome regarding patient age.(1)

Xerostomia is one of the most prevalent late side effects of radiation for head and neck malignancies, and patients cite it as the major cause of decreased quality of life. The degree of xerostomia has been reported to depend on the radiation dose and volume of salivary gland irradiated.

However, radiation of young patients has specific implications given their potential lifespan. As patients survive longer after radiation treatment for HNC, the long-term consequences of this treatment become more significant.

Objectives

To evaluate the radiation side effects and determinants among HNC patients at ORCI for the past two years attendig follow up clinic at ORCI hospital between May and September 2012. Also to determine the most prevalent cause of radiation of side effect.

Methodology

This was a Cross Sectional Descriptive Study.Setting was at ORCI involved 72 consented subjects. Characteristics of the type of radiation side effects and determinants was noted and documented in the request form. Collected data was analyzed using SPSS V15. For the continuous data mean and standard deviation will be considered while for the categorical is by number and percent. The association between radiation side effects and determinants was established using chi square.

Budget

The whole process from data collection to report submission will cost 1,515,000 Tanzanian shillings.

Results

A total of 72 patients were included in the study with majority being >65 years of age. SCC was the leading histological type seen in these patients.The study showed that 61.1% of the patients included in the study were not staged. Mucositis was seen as the commonest radiation side effect reported in 50% of the patients. CRT was not associated with increase in radiation side effect compared to EBRT alone.

The APPA field technique that was given in most patients resulted in more radiation side effect compare to three separate field technique which was given to some few patients.

Conclusion and Recommendations

Successful treatment of HNSCC needs planned combination of different treament modalities to achieve local tumor control with minimal radiation side effect.The use of new generation machines increase radiation dose to the target and minimizes doses to critical organs.

Oral hygiene and adequate nutrition during RT coarse can be helpful in minimizing radiation side effect in absence of anti-mucositic agents.

TABLE OF CONTENT

LIST OF TABLES

LIST OF ABBREVIATIONS

HNC	Head and neck cancer
HNCC	Head and neck squamous cell carcinoma
CT	Conventinal Radiotherapy
HPV	Human Papilloma Virus
RT	Radiotherapy
CRT	Concurrent Chemoradiotherapy
DVH	Dose Volume Histogram
APPA	Anterior-Posterior, Posterior Anterior
EBRT	External Beam Radiotherapy
3D CRT	Three Dimension Conformal Radiotherapy
IMRT	Intensity Modulated Radiotherapy
LINAC	Linear Accelerator
IARC	International agency for Research Cancer
ORCI	Ocean Road Cancer Institute
RTGO	Radiotherapy Oncology Group
CTC 2.0	Common Toxicity Criteria version 2

CHAPTER ONE

INTRODUCTION

1.1 Background

HNC describe malignant tumours arising in the upper aerodigestive tract including the oral cavity, larynx, and nasopharynx. HNC is remarkable for its ability to cause extensive tissue damage and regional node involvement in absence of distant metastasis(2).

The spectrum of malignant tumour that affect HNC are:

1. **Surface epithelium**- SCC in 90 percent of the cases.
2. **Glandular epithelium –** adenocarcinoma in females and mucoepidermoid cancer in males.

3. **Mesenchymal tissues-** lymphomas and sarcomas are very rare**.**

Etiology and Risk Factors:

Tobacco and alcohol

Several authors have found there is a lower rate of tobacco and alcohol use among young HNSCC patients compared with older HNSCC patients(3) however, others found no difference in use (4) In a review of risk factors in 116 patients from the south east of England, Llewellyn et al found equal and substantial exposure to tobacco and alcohol in young patients with oral SCC and a control group of patients without cancer. In their analysis, tobacco consumption for greater than 21 years resulted in a significantly elevated risk of oral cancer(5).

Human papillomavirus

The most widely studied virus in HNC literature in recent years is HPV, a virus initially linked to cervical carcinogenesis that has now gained interest for its connection to cancer of the oropharynx, particularly the lingual and palatine tonsils(6)

The increasing incidence of tongue and tonsil cancer among young patients suggest that HPV may be responsible for this trend although the connection between oral versus oropharyngeal cancer and HPV is controversial(7,8)

A case control analysis looking at HPV-16 status of 240 patients with HNSCC at Johns Hopkins, found a higher proportion of young patients (< 50 years) in the HPV-16–positive group than the HPV-16–negative group 33% vs 17%, respectively(9). Additionally, they found a strong association between HPV-16 positivity and oropharyngeal and lingual or palatine tonsil primary sites.

Human immunodeficiency virus

Infection with the human immunodeficiency virus (HIV) and progression to AIDS is positively correlated with malignancies of the upper aerodigestive tract, particularly Kaposi sarcoma and non- Hodgkin's lymphoma,to a lesser extent SCC (10)

Types of Head and Neck Cancer

Cancer can develop in several different parts of the head and neck. Some of the most common include the following:

Oral Cancer

Cancer of the oral cavity (mouth) is the most common type of head and neck cancer. It begins in the lips, the inside of the lips and cheeks, the floor and roof (hard palate) of the mouth, and the front of the tongue. The main risk factors for oral cancer are smoking or chewing tobacco and excessive alcohol use.The most common symptoms include a sore or lump on the lip or in the mouth that does not heal; a white and/or red patch on the gums, tongue, or cheeks ; unusual or persistent bleeding, pain, and swelling that causes dentures to fit poorly or become uncomfortable.

Laryngeal Cancer

Laryngeal cancer, arises in the larynx (voice box) and is the second most common type of head and neck cancer.The vast majority of laryngeal cancers occur in men. Tobacco and alcohol use are the most common risk factors for laryngeal cancer.

Additional risk factors include exposure to wood and metal dusts, asbestos, paint fumes, and other chemical inhalants; a diet low in vitamins A and E; gastroesophageal reflux disease (GERD), which chronically expose the throat to acidic stomach contents. The most
common symptoms of laryngeal cancer include hoarseness, a lump in the neck (due to an enlarged lymph node), ear pain, and difficulty in swallowing.

Pharyngeal (Throat) Cancer

Pharyngeal cancer arises in the pharynx (throat). Tumors in this region include cancers of the nasopharynx, oropharynx and hypopharynx.

Nasopharyngeal Cancer

The nasopharynx, located behind the nose, includes two openings that lead to the ears. Risk factors for this type of cancer include a diet high in salt-cured fish and infection with Epstein-Barr virus, a member of the herpesvirus family and one of the most common human viruses. The most common sign of nasopharyngeal cancer is a lump in the neck, caused by the spread of cancer to the lymph nodes.

Oropharyngeal Cancer

The oropharynx is located behind the mouth and includes the base of the tongue, the soft palate (the soft area just beyond the roof of the mouth), and the area around the tonsils. Smoking and chewing tobacco and heavy alcohol use are the most common risk factors for oropharyngeal cancer. Prior infection with human papillomavirus (HPV) is also a particularly strong risk factor for this cancer site. Symptoms of oropharyngeal cancer may include a lump in the neck or throat, persistent sore throat, hoarseness, difficulty in swallowing, and ear and/or jaw pain.

Hypopharyngeal Cancer

The hypopharynx is the uppermost portion of the esophagus and surrounds the larynx (voice box). As with most other HNC, tobacco use and heavy alcohol consumption are the most common risk factors. Other risk factors for hypopharyngeal cancer may include a diet low in vitamins A and E; exposure to asbestos, wood dust, paint fumes, and other inhalants; and Plummer-Vinson syndrome (a rare condition that causes difficulty in swallowing). Symptoms of hypopharyngeal cancer may include a lump in the neck, hoarseness, difficulty in swallowing, and ear pain.

Head and Neck Cancer Staging

- **Primary tumour**- indicated by letter T and suffix that represent more advancing disease.

  i) T1- Tumor 2 cm or less

  ii) T2 – Tumour more than 2 cm less than 4 cm

  iii) T3 – Tumour more than 4 cm

  iv) T4 – Tumour more than 4 cm with deep invasion of underlying tissue.

- **Lymphnode**- assess the progression of lymhnode involvement.

  i. N1- Single ipsilateral nodes 3 cm or less in diameter.

  ii. N2- Single ipsilateral nodes more than 3 cm but less than 6 cm, or multiple clinically ipsilateral less than 6 cm.

  N2a-Single

  N2b-multiple.

iii. Clinically positive ipsilateral nodes more than 6 cm, bilateral or contralateral.

N3a- ipsilateral more than 6 cm

N3b- bilateral each side staged separately

N3c- contralateral only.

- **Distant metastasis**

M0 – no metastasis present.

M1 – metastasis clinically demonstrable

Mx – metastasis cannot be assessed**.**

TNM Staging

a) Stage 1: **T1,N0,MO**

-Compromise negative node and an operable primary.

b) Stage 2: **T2,N0,M0**.

- Operable primary tumour with operable node.

c) Stage 3: **T3,N0,M0** and **T1,2 or 3, N1, M0**

-Inoperable primary tumour and nodal involvement which is advanced

d) Stage 4:**T4, N0 or 1**, M0, **T1-4, N2 or 3, M0and T1-4, N1-3, M1**- Distant metastasis that may not need any surgical intervention.

HNC may be further divided into 3 clinical subgroups:(11)

1. Localized disease which is a stage 1 or 2 disease
2. Local regional advance disease with large primary tumour and/ or lymphnode metastasis.
3. Recurrent or metastatic disease which approximates one third of HNC patients with localized disease .

Treatment and Management

Chemotherapy and radiation therapy

Radiation is used as single modality therapy for early stage disease (stage I-II) and in multimodality therapy for advanced disease (stage III-IV) and may be used alone or in combination with surgery and chemotherapy for the treatment of HNC .

The objective of radiation therapy is to maximize the probability of cure with a minimum of side effects. Radiation therapy is considered a local treatment because only the cancer cells in the area of the body where the radiation is delivered are killed.

The most common ways in which radiation therapy is delivered are externally, through external beam radiation therapy which involves the delivery of radiation via a machine that aims x-rays at the body.

Patterns of recurrence

Several small case series have been published reporting young patients with a high rate of locoregional recurrence and could be a lack of appropriate initial surgical treatment. Because of their young age, these patients may not have been as aggressively treated as their older counter parts(12)

Second primary tumors

In patients of all ages who have been treated for HNSCC, the risk of development of second primaries increases over time(13) and is linked to tobacco consumption. A matched control study found a decreased incidence of second primaries among patients younger than 40 years compared with older patients (8% versus 18%) over 10 years, but this may have been confounded by the higher proportion of smokers in the older age group.(14)

1.2 Literature Review

Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer worldwide and treatment protocols including radiation combined with chemotherapy, EBRT alone and surgery, may all result in tremendous patient morbidity.(15)

Despite continuing research and advances in treatment, the clinical outcomes and overall survival rates for HNSCC have not improved significantly over the last several decades, with the overall 5 year survival rate as low as 50% (16- 18). As a result, there has been continuing investigation into potential alternative and less toxic therapies for HNC, with the aim of achieving a more favorable clinical outcome while reducing treatment morbidity. Although HNSCC generally remains more common in males, even among young patients, some studies have reported a higher relative incidence in females.(19)

EBRT combined with chemotherapy is associated with systemic toxicities that often reduce compliance and prevent timely completion of therapy and accounts for many long-term side effects(20). Early stage (stage I and II) tumors are treated primarily by single modality with either surgery or radiotherapy, with both modalities resulting in similar local control and survival rates. More advanced (stage III and IV) 66% cancers often require multi-modality therapy with surgery, radiation and chemotherapy which can result in very high morbidity.(21,22)

Radiation effects on normal tissues are divided into acute(early) and chronic (late) effects. Acute effects occur during the course of therapy and during the posttherapy period

(approximately 2-3 weeks after the completion of a course of irradiation). Chronic effects can manifest anytime thereafter, from weeks to years after the treatment.(23)

Modern radiation therapy for HNC is usually administered with linear accelerators, which produce high-energy external radiation beams. This beam of radiation penetrates the tissues and delivers the radiation dose deep in the area of the body where the cancer resides and have enabled radiation oncologists to significantly reduce side effects while improving the capacity to deliver radiation to the cancer.(24)

A typical course of radiation for cancer of the head and neck lasts 3-5 weeks with daily treatments from Monday through to Friday. However, rapidly growing cancers are poorly controlled if radiation is given in daily doses over a long period of time. Therefore, delivery of radiation can be accelerated and given in two or more treatments per day (hyperfractionation) for certain rapidly growing HNC such as nasopharyngeal cancers (24) and has significantly better local-regional control and improved disease-free survival(25) than treatement with standard fractionation.

Another study suggests that there is some moderate evidence that accelerated hyperfractionation treatment reduce serious late side effects while retaining a similar tumour effect as standard single fraction modality in rapidly growing cancers(26).

Side Effects and Complications:

The most significant immediate side effects of radiation for HNC are mucositis, inflammation of the mucous membranes of the mouth or throat, and dry mouth (xerostomia) (24). Difficulties with xerostomia, fibrosis, and swallowing are significant quality of life issues in long-term survivors HNC irradiation(1) and is usually complete after modest doses of radiation to the parotid glands. With doses of 40-60 Gy, fewer than 20% of patients have a measurable salivary flow. With doses lower than 30 Gy, some function may return after 6-12 months. However, at doses exceeding 50 Gy, xerostomia is usually irreversible.(27)

Late dysphagia after chemoradiotherapy for locally advanced HNSCC motivate further efforts to reduce the dose to the swallowing structures, especially to the pharyngeal constrictor muscles and the larynx. (28)

Treatment with radiation can damage healthy tissues to the point that a second cancer may develop. In the head and neck area, radiation treatment for a primary cancer is a frequent cause of second cancers. Thus, the risk of receiving radiation therapy must be carefully weighed with the benefit.(24)

Osteoradionecrosis of bones within the radiation field (most commonly the mandible) may occur as a result of damage to the bone vasculature and osteocytes and is one of the most serious complications of radiotherapy(29).

Strategies to Improve Radiation Treatment of Head and Neck Cancers

The development of more effective cancer treatments requires that new and innovative therapies be evaluated with cancer patients(24). Areas of active exploration to improve radiation treatment of HNC include the following:

Three-Dimensional Conformal Radiation: Three-dimensional conformal radiation therapy is a promising approach for the treatment of HNC because it decreases the exposure of normal tissues to radiation and has a good target coverage, also allows high-dose external beam radiation therapy to be delivered primarily to the cancer with less damage to normal cells. The technique is particularly useful in the treatment HNC near the midline of the body because conventional radiotherapy usually damages the salivary glands resulting in xerostomia, or dry mouth.(24)

Clinical studies have demonstrated that salivary glands could be spared from radiation damage with the conformal radiation technique and resulted in significantly less radiation to the salivary glands and improved doses of radiation delivered to the target cancer cells compared to conventional external beam radiation therapy.(24)

Acceleration of Radiation Dose: A clinical trial showed that the risk of a local cancer recurrence may be reduced in patients with locally advanced HNC by using increased frequency and doses of radiation therapy. Over 1,000 patients received radiation therapy either once daily or twice daily. Higher doses of radiation were delivered to the group of patients receiving treatment twice daily, whereas standard doses of radiation were delivered to the group of patients receiving treatment once daily. Two years following treatment, 56% of patients receiving radiation treatment twice daily were free of cancer recurrence, compared with 46% of patients who received radiation once daily.(24)

Radiation Protectors: Radiation protectors are drugs that selectively protect normal tissues from radiation treatment, while exposing cancer cells. Clinical data suggest that patients receiving Amifostine during radiation therapy can reduce both early and late radiation-induced side effects. Amifostine has a radioprotective effect on salivary gland and minimize mucositis(24)

In a large multi-center clinical trial, 300 patients with HNC received either radiation therapy combined with Amifostine or radiation therapy alone. Xerostomia occurred in 51% of patients receiving amifostine compared to 78% for patients receiving radiation therapy without amifostine. One year following completion of radiation therapy, only 35% of patients who had received amifostine were still experiencing symptoms of xerostomia, whereas 57% of patients who had received radiation therapy alone were still experiencing the symptoms.(24) Another study suggest that there is insufficient evidence that radioprotective agents offer clinically significant protection of parotid glands or spare tumour tissue. (30)

Radiosensitizers: Radiosensitizers are drugs that make cancer cells more susceptible to damage by radiation therapy. Cancers with low levels of oxygen are less sensitive to radiation than cancers with normal or high levels. A radiosensitizer drug, Nimorazole, significantly improved the effect of radiotherapeutic management of HNC without major side effects. In this clinical trial 144 patients with pharynx and larynx carcinoma were treated. Half the patients received the radiosensitizer and half received placebo.

All patients received conventional radiotherapy. Overall, the group that received the radiosensitizer experienced significantly better local and regional control of cancer and lived longer. Drug-related side effects were minor and tolerable, the most common of which were transient nausea and vomiting.(24)

1.3 Problem Statement

Head and neck squamous cell carcinoma (HNSCC) typically develops in the sixth to seventh decade of life. Clinicians have become increasingly aware of patients who develop HNSCC at a young age, variably defined as age 30 years and younger, 40 years and younger, or 50 years and younger.(31)

Radiotherapy is generally used in the treatment of malignant tumors in the head and neck region. It causes a hypoxic, hypocellular, and hypovascular environment that leads to injury to surrounding normal tissue, both acute and chronic, ranging from xerostomia to osteoradionecrosis. Cure rates among HNC are still low (32), and current treatment regimens are not aiming at reducing the radiation side effects and hence improving the quality of life and survival among HNC patients. These side effects are debilitating and greatly influence quality of life in these patients.The burden of managing the radiation side effects is enormous. More than half of these persons are in the developing world.(31)

About 200 cases of HNC on average were seen per year at ORCI between 2006 and 2009. Patients received at advance stage with advance primary tumor stage (T3 or T4) thus resulting in severe radiation side effects. This study will identify the magnitude of the radiation side effects and their determinants and how they contribute to poor quality of life and increase in toxicity among HNC patients.

The HNC treatment at ORCI is faced by challenges of compromised tolerance to treament due to poor nutritional status and weight loss and treatment induced mucositis. Also the close proximity of the tumor to critical organs thus most of the total dose delivered is limited by tolerance of normal structures.

A number of studies in the developed world have shown that patients with HNSCC who are treated with RT develop radiation side effects such as mucositis, skin reactions and soreness inside mouth. However few studies have assessed this problem in Africa and particularly in Tanzania there is no study that has assessed the magnitude of radiation side effects and their deteminants among patients with HNSCC.

1.4 Rationale

In developing countries such as Tanzania, strategies to improve radiation treatment such as three-conformal dimension and acceleration dose radiation have been sidelined due to financial implications. Understanding the prognostic indicators will help to determine the magnitude of radition side effects and their determinants and its associated morbidities that are caused by radiotherapy. Also many of the early tumors are curable if diagnosed early and appropriate radiation therapy is given.

There is also a challenge on how to get an appropriate therapeutic window that maximizes tumor cell kill while minimizing normal tissue injury. In our setting we concentrate on improving survival and local tumor control but allow for greater severity of mucosal injury.

There are no scientific researches that have been done at ORCI to show the radiation side effects and its determinants among HNC patients. This study is expected to find the different types of radiation side effects and the type of treatment modality in relation to the disease profile. Absence of research studies and information on detrminants of radiation side effects indicate a need to conduct this study at ORCI.

Results will assist in improving care and minimizing the radiation side effects so as to improve the quality of life and improve prognosis. Patient will be treated according to disease profile so as to improve the standard treatment.

1.5 Objectives

1.5.1 Broad Objective

To determine the magnitude of radiation side effects among HNC patients diagnosed in the past two years attendig follow up clinic at ORCI hospital between May and September 2012.

1.5.2 Specific Objectives

1. To determine the demographic characteristics distribution and disease profile among HNC patients that attended follow up clinic between May- September 2012.

2. To determine the relationship between the modality of treatment used and radiation side effect in HNC patients that attended follow up clinic between May and September 2012.

3. To determine the relationship between social demographic characteristics and radiation side effects among HNC that attended follow up clinic between May and September 2012

HYPOTHESIS:

Null hypothesis: There are no radiation side effects among patients with HNC.

Alternative hypothesis: There are radiation side effects among patients with HNC

CHAPTER TWO

METHODOLOGY

2.1 Type of Study

This was a Cross Sectional Descriptive Study. This study involved determining the causes of radiotherapy side effects in HNC patients that attended follow up clinic at ORCI. The study duration was from May –September 2012.

2.2 Study Area/ Study Population

The study was conducted at ORCI in the follow up clinics between May and September 2012. The study included 72 consented patients with HNC that had completed radiotherapy. They were assessed for determinants of radiotherapy side effects in relation to treatment modality they received. Patients with other malignant condition in the head nd neck such as eye, ear or brain were not included in the study.

2.3 Sample Size Estimation

Sample size was calculated based on the estimated proportion of 0.54 and 0.17 respectively of HNC patients with radiation side effects following radiotherapy treatment. Using double sided test P 0.05 and power of 90% a sample size of 45 patients was reached. A figure of 72 patients was taken so as to do away with failure of some patient files to be retrieved for the follow up clinic.

2.3.1 Inclusion Criteria

All HNC patients who had consented and attended follow up clinic between May and September 2012 after radiotherapy treatment were assessed for radiotherapy side effects and determinants of the side effects.

2.3.2 Exclusion Criteria

All HNC patients categorized with other malignant tumours in the Head and neck region such as the eye, brain or ear and attended follow up clinic between May and September 2012 were not included in the study. HNC patients with no confirmed histopathology report were also excluded from the study.

2.4 Sampling Technique

All HNC patients treated with radiotherapy who had attended follow up clinic between May and September 2012 were evaluated for the side effects of radiotherapy and the determinants of the side effects.

2.5 Data Collection

Evaluation of clinical toxicity was made according to the Radiation Therapy Oncology Group (RTOG) acute and late morbidity scoring system that classifies toxicity of patients into different levels: grade I (mild) to grade IV (severe).

Also, Common Toxicity Criteria Version 2(CTC 2) was used to classify common toxicity such as dysphagia and fatigue related to xerostomia.

This was monitored during the second week of treatment and at the end of treatment.Recovery and healing were assessed during the follow up clinic 3 weeks after the last day of RT.

An informed consent was obtained to allow for the radiotherapy prescription form to be used in the study. Treatment modality (technique, total dose and daily dose) were also obtained from the radiotherapy prescription form

A short interview was conducted to obtain demographic data. This was conducted by the chief investigator.

2.6 Data Analysis / Implementation Plan

The data analysis was done using the SPSS info program version 15 and cox regression by multivariate analysis, analyzing data focusing on the findings of determinants of radiotherapy side effects, the association between the radiation side effect and clinical factors such as mode of treatment and field technique. The p-value and odds ratio were the index for the null hypothesis and 95% CI respectively. The observed outcome was considered to be statistically significant.

2.7 Ethical Clearence

Ethical clearance to conduct the study was obtained from MUHAS Ethical Commitee and the Management of ORCI to use patients as study subjects and also patients' records to determine the side effects of radiotherapy. The informed consent was obtained from the study subjects.

2.7.1 Disposal of Study Patients

All HNC patients with side effects following radiotherapy treament encountered during the study were immediately sent to Radiation Oncologist to continue with the necessary intervention.

2.8 Dissemination of Results

The results obtained from this study which is part of partial fulfillment of the Masters of Medicine in Clinical Oncology, will be presented to Muhimbili University of Health and Allied Sciences. In addition the hospital authority will also be notified on the findings obtained and the results presented in scientific meetings and published in local and international journals.

CHAPTER THREE

RESULTS

Table 1: Socio and demographic distribution of patients presenting radiation side effects.

(N=72)

Characteristics	Frequency	Percentage
Age		
25-44	17	23.6
45-64	27	37.5
>65	28	38.9
Sex		
M	47	65.3
F	25	34.7
Level of Education		
No Formal Education	37	51.4
Primary Education	24	33.3
Secondary Education	10	13.9
Post Secondary	1	1.39

The age study population ranged from 25 to 90 years. The most prevalent age group was 65 and above (38.9%). Also there were more males (65.3%) compared to females(34.7%) (Percentage in the parenthesis).Most of the patients had no formal education(51.4%) and 33.3% had at least primary level of education.

Table 2: Clinical Characteristics of the disease of patients with radiation side effects(N=72)

Clinical Characteristics	Frequency	Percentage
Stage		
II	2	2.8
III	11	15.3
IV	15	20.8
Unknown	44	61.1
Histology		
SCC	56	77.8
Adenoid Cystic	10	13.9
Mucoepidermoid	5	6.9
Follicular	1	1.39

The study findings show that most of the HNC were diagnosed stage IV(20.8%) , stage III(15.3%) and most patients were not staged (61.1%).

SCC was the leading histological type confirmed(77.8%) while other histological type like Adenoid cystic(13.9%), Mucoepidermoid (6.9%) and only about 1.39% had Follicular carcinoma.

Table 3: Percentage distribution of radiation side effect and treatment modality (N=72)

	Frequency	Percentage
RTGO Criteria		
Mucositis		
Grade I	3	8.3
Grade II	10	27.8
Grade III	22	61.1
Grade IV	1	2.8
CTC 2.0 Criteria		
Dysphagia	28	38.9
Xerostomia	19	26.4
No side effect	8	11.1
Mode of Treatment		
EBRT alone	38	52.8
EBRT + radiosensitizer	34	47.2

The study showed increased toxicity in patients treated by chemoradiation, mostly grade III(61.1%) mucosal toxicity. In 10 patients, the mucosal reactions were grade II(27.8 %) with only one grade IV(2.8%).Dysphagia was seen in 28 (38.9%) patients, (11.1%) developed no w radiation side effect. The acute reactions healed within three months from the last day of radiotherapy.

Table 4: Percentage distribution of radiation side effects by sociodemographic characteristic (N=72)

		Radiation Side Effect	X2 (P value)
Age	Yes	No	5.885(0.119)
<64	37(84.1)	7(15.9)	
>64	27(96.4)	1(3.6)	
Sex			2.271(0.581)
M	40(62.5)	4(50.0)	
F	24(37.5)	4(50.0)	
Level of Education			18.809(0.093)
No formal Education	55(85.9)	5(62.5)	
Post Primary	9(14.1)	3(37.5)	

The study findings showed that out of patients with radiation side effect, males had more side effects(62.5%) compare to females(37.5%).The age group that had more radiation side effect was 64 and below(84.1%). Majority of patients(93.4%) with either primary level of education or no formal education had radiation side effect.

Table 5: Percentage distribution of radiation side effects by treatment modality and treatment field technique (N=72)

	Radiation Side Effect		X2(P value)
Mode of treatment	Yes(%)	No(%)	0.341(0.559)
EBRT alone	33(86.8)	5(13.2)	
EBRT + radiosensitizer	31(91.2)	3(8.8)	
Field Technique			
APPA	45(97.8)	1(2.2)	2.924(0.0403)
Latopp,Antlas, Dirant.	19(73.1)	7(26.9)	

Patients treated by EBRT and radiosensitizer had more radiation side effect(91.2%) compare to those treated by EBRT alone. Majority of the patients treated by APPA (97.8%) had radiation side effect compared to other treatment field technique(73.1%).

Table 6: Odds ratio of radiation side effects, sociodemographical and clinical factors Among HNC with radiation side effect.

	Radiation Side Effect		OR (95%CI)	P-value
	Yes(%)	No(%)		
Age				
< 64	37(84.1)	7(15.9)	1	
>64	27(96.4)	1(3.6)	5.1(0.57-11.7)	0.61
Sex				
M	40(62.5)	4(50.0)	1	
F	24(37.5)	4(50.0)	0.83(0.1-5.93)	0.09
Level of Education				
No formal Education	55(85.9)	5(62.5)	0.31(0.04-1.78)	0.11
Post Primary	9(14.1)	3(37.5)	1	
Mode of treatment				
EBRT alone	33(86.8)	5(13.2)	1	
EBRT +radiosensitizer	31(91.2)	3(8.8)	0.72(0.11-3.45)	0.59
Field technique				
APPA	45(97.8)	1(2.2)	8(2.8-38.4)	0.002
Latopp,Antlas, Dirant	19(73.1)	7(26.9)	1	

In multivariate analysis(Table 7.6). The position association between radiation side effect and field technique remained the same,where patient treated by APPA field technique were eight times more likely to get radiation side effect compared to other treatment field technique like lateral opposed and direct anterior.However, there was no significant association in odds ratio to other clinical factors above as in the univariate analysis.

CHAPTER FOUR

DISCUSSION

In general, conventional radiotherapy involves the delivery of fractionated radiation (commonly 2 Gy daily to 70 Gy) and is complicated by the close proximity of tumour and normal tissue structures such as the spinal cord. . Normal tissue toxicity induced by conventional radiotherapy is the main limiting factor in the treatment progress.

Patients treated with conventional radiotherapy developed clinical toxicity and this limited the success of the treatment (32). Also,the genetic and molecular mechanisms of therapeutic radiation sensitivity are still poorly understood (33-34).

However, in this study patients tolerated treatment and received the intended dose of radiation therapy.

Attempts to improve on both the efficacy and toxicity profile for head and neck radiotherapy led to the development of a number of alternative delivery schedules, employing different fractionation regimens(35)

Studies have shown patients treated with hyperfractionation and accelerated fractionation with concomitant boost had significantly better local-regional control than those treated with standard fractionation(36).

Hyperfractionation involves the use of multiple smaller dose fractions (<2 Gy) delivered at an increased frequency (commonly twice daily), affording an increase in the total dose delivered over the same time as conventional radiotherapy, but with equivalent long-term toxicities.

All patients were treated by standard fractionation therapy using a 2 dimension cobalt 60 machine with majority(64%) being treated by two separate field technique, APPA to a total of 50 Gys and a few(36%) by other field techniques such as lateral opposed, direct anterior and anterior lateral. A study(37) showed that stage III and IV HNC were treated by at least three separate field technique using 3DCRT to a total dose of 70 Gys and allowed delivery of high dose to the target area while sparing the normal tissues and critical organs and therefore minimal radiation side effects.

.In this study all patients were given conventional fractionated RT with single daily doses

(hypofractionation) between 1.8-2.0 Gys , 5 times a week to a total of 2, 3 or 5 weeks. Single daily doses (hypofractionation) resulted in increased complication and decreased local tumor control(38)

In this crossectional study, the most prevalent age group with radiation side effect was >65 years. This is similar to a study done by Syrigus K.N at Sotiria Medical Centre (39) whereby the median age of diagnosis was in sixth decade. A study byMckoy, J.M in North Western University(40) was conducted on elderly HNC patients above 65 years. The study findings showed that there were more males(65%) compared to females (35%) and a study by Parkin, D.M et al(41) at IARC showed large male to female predominance.

In this study population majority of the patients (51.4%) had not been to school and this could have contributed to late presentation of the disease at ORCI.
The study further revealed that out of 72 patients,61.1% were reffered to ORCI with no surgical staging, 20.8% were stage IV and very few (2.8%) were stage II.
SCC was the leading histological type (77.8%), similar to the study by Van den Brook Cetal at Gustave Institute which showed that 90% of HNC patients were SCC.

. This acute adverse effect may be patient or treatment related. Patient factors such as age, sex, oral heath, use of tobacco contributed to mucositis. Also treatment factors like surface area/ volume of the head irradiated, rate of dose accumulation (fractionation), concurrent radiosensitizer use and two dimension Cobalt 60 and field technique.(42)

The most common and clinically significant radiation side effect reported majority of the patients was mucositis 50%(grade II and III) .Other severe toxicity were such as tooth decay and skin reactions were infrequent even at higher radiation doses

In this study grade III toxicity was mostly encountered (61.1%) which were majority of the patient and this was observed at the primary site of the tumor. In 10 patients (27.8%) mucosal toxicity were recorded as grade II. No grade I mucosal reactions were noted and only about 1(2.8%) had grade IV mucosal toxicity.

Similar study (43) showed increase toxicity in protocol that use concurrent chemotherapy mostly grade II (38%) and III(62%) mucosal toxicity with no grade IV mucosal toxicity noted and this calls for research on toxicity relieving therapies(44).

Oropharyngeal mucositis was noted as the most significant side effect in head and neck cancer. Conventional fractionation with two field geometry showed severe mucosal reaction in the second week of RT towards the end. Recovery occurs within three weeks from the last day of RT and mucosa heals in 90 % to 95 % of patients(45).

Acute mucosal reactions caused pain, difficult in speaking and eating which may be worsened by nutritional status and weight loss that resulted in significant loss of tumor control and interrupted RT schedule dose(46).

However, in this study marked improvement was seen in HNC patients during their follow up visits 3 months post EBRT with both general function and physical measure returned to baseline level.

Xerostomia was seen in 26.4% of the study population this could be due to RT induced salivary gland damage caused by the use of two dimension machine with two separate field technique instead of three separate field technique. The loss of salivary gland function reduced quality of life and impair social activities for long term survivors. Also mouth dryness can also result to dental decay and nutritional problems.(47)

In this study radiation side effect was reported more in patients treated with EBRT alone(51.4%) compared with (48.6%) of patients treated by EBRT and chemotherapy cisplatin was used as radiosensitizer.

Socio demographic characteristics in terms of sex (*p* value 0.5810), age group (*p* value 0.1190) and level of education(*p* value 0.093) did not show association with radiation side effect. A study by Van der Meulen at Utrech University showed that the level of education was not related to outcome of radition side effect. Statistical finding of (*p* value 0.558) showed no association of CRT with radiation side effect as more side effect were seen in patients who were treated by EBRT alone. This could be explained by the fact that patients' related factors such as old age, poor nutritional status contributed to more radiation side effect to patients treated by EBRT alone. At the same time, most of the patients with advance disease and who were not staged had received high dose EBRT alone and this could have contributed to more severe radiation side effect.

There was association between the treatment field technique and radiation side effect (*p* value 0.0403). The APPA field technique that was given in most patients resulted in more radiation side effect specifically mucosal reaction compare to three separate field technique which was given to a few of the patients. New technology machines can provide high dose to the target volume while sparing the nearby critical organs.

There was apparent association between radiation side effect and field technique which remained the same as in univariate analysid(p-value 0.002) and 95% CI(2.8-38.4) whereby patient treated by APPA field technique were eight times more likely to radiation side effect compared to other field technique like lateral opposed and direct anterior therefore it was important to use three field technique so as to minimize radiation side effects.

However, there was no significant changes in the odds ratio to other clinical factors that were associated to radiation side effect such as age, sex, level of education and mode of treatment.

CHAPTER FIVE

STUDY LIMITATION

1.The study sample was not representative of the general population of HNC patients with radiation side effect and the fact patients were recruited only from ORCI; increased the bias.

2.There were very few patients diagnosed with HNC in the year 2010 that attended follow up clinic between May 2012 and September 2012 and this made difficult to draw conclusion clearly on the magnitude of radiation side effect in HNC patients diagnosed in year 2010.

3.Grading toxicity by RTGO criteria based on physician grading does not necessarily reflect patient burden of symptoms.

CONCLUSION

- HNC that received EBRT and radiosensitizer suffered from more radiation side effect during their coarse of treatment compared to patient treated with EBRT alone.
- Currently we try to limit the severity of radiation side effects by proper planning and simulation, use of supportive and palliative care like use of anaelgesics and basic oral care.
- The association between radiation side effect and tumor response can be confirmed in future prospective clinical trials as well as translational biomolecular research, this will be another promising step into individualized personal tumor therapy with dose adapting treatment regimens depending on pretreatment analysis and evaluation of toxicity during radiation therapy.

RECOMMENDATION

- Careful oral hygiene and adequate nutritional status during radiotherapy coarse can be helpful in reducing radiation side effect.
- We need a surgeon at ORCI so as to help in staging of the patients since many of patients in this study were not staged.
- Treatment simulation can reduce errors in patient positioning and help in field localization hence reduce radiation side effect. Also the use immobilization devices will help reducing radiation side effect.
- New generation machines such as LINAC enable high doses to be given by producing sharp field edges, also IMRT enable irrregular shaping of the target volume

REFFERENCES

1. Langendijk JA, Doornaert P, Verdonck-de Leeuw IM, et al. *Impact of late treatment-related toxicity on quality of life among patients with head and neck cancer treated with radiotherapy.* J Clin Oncol. Aug 1,2008;26(22):3770-6.

2. HNC PPT: *AJCC*.1983

3. Schantz SP, Byers RM, Goepfert H, Shallenberger RC, et al**.** *The implication of Tobacco use in the young adult with Head and Neck Cancer*.Oct 1 1988;62(7):1374-80.

4. Pytynia KB, Grant JR, Etzel CJ, et al. *Squamous cell carcinoma of the oral cavity in patients aged 45 years and under: a descriptive analysis of 116 cases diagnosed in the South East of England from 1990 to 1997.* Oral Oncol. Feb 2003;39(2):106-14.

5. Llewellyn CD, Linklater K7, Sturgis EM, et al. *Matched analysis of survival in patients with squamous cell carcinoma of the head and neck diagnosed before and after 40 years of age.* Arch Otolaryngol Head Neck Surg. Jul 2004;130(7):869

6. Gillison ML. *Current topics in the epidemiology of oral cavity and oropharyngeal cancers*. Head Neck. Aug 2007;29(8):779-92)

7. Shiboski CH, Schmidt BL, Jordan RC, et al. *Tongue and tonsil carcinoma: increasing trends in the U.S. population ages 20-44 years.* Cancer. May 1 2005;103(9):1843-9.

8. Schantz SP, Yu GP. *Head and neck cancer incidence trends in young Americans, 1973-1997, with a special analysis for tongue cancer*. Arch Otolaryngol Head Neck Surg. Mar 2002;128(3):268-74.

9. Gillison ML, D'Souza G, Westra W, et al**.** *Distinct risk factor profiles for human papillomavirus type 16-positive and human papillomavirus type 16-negative Head and Neck Cancers.* J Natl Cancer Inst. Mar 19 2008;100(6):407-20.

10. Epstein JB, Silverman S Jr. *Head and neck malignancies associated with HIV infection.* Oral Surg Oral Med Oral Pathol. Feb 1992;73(2):193-200).

11. Jennifer M Lee, Marco Turini, Marc F Botteman, et al**.** *Economic burden of Head and Neck Cancer.*

12**.** Sarkaria JN, Harari PM**.** *Oral tongue cancer in young adults less than 40 years of age*: *rationale for aggressive therapy*. Head Neck. Mar-Apr 1994;16(2):107-11.

13. Argiris A, Brockstein BE, Haraf DJ, et al. *Competing causes of death and second primary tumors in patients with locoregionally advanced head and neck cancer treated with chemoradiotherapy.* Clin Cancer Res. Mar 15 2004;10(6):1956-62.

14. Verschuur HP, Irish JC, O'Sullivan B, et al**.** *A matched control study of treatment outcome in young patients with squamous cell carcinoma of the head and neck.* Laryngoscope. Feb 1999;109(2 Pt 1):249-58.

15. Epstein JB, Robertson M, Emerton S, et al. *Curcumin: A study of patients with Head and Neck Cancer*: A feasibility study including the EORTC QLQ- C30.

16. Stell PM.*Survival time in end-stage Head and Neck Cancer*. Eur J Surgical Oncol 1989; 15:407-10.

17**.** Vokes EE, Weichselbaum RR, Lippman SM, et al. *Head and neck cancer*.N Engl J Med 1993, 328:184-194.

18. Argiris A, Brockstein BE, Haraf DJ, et al**.** *Competing causes of death and second primary tumors in patients with locoregionally advanced head and neck cancer treated with chemoradiotherapy*. Clin Cancer Res 2004:10:1956-1962.

19. Martin-Granizo R, Rodriguez-Campo F, Naval L, et al. *Squamous cell carcinoma of the oral cavity in patients younger than 40 years.* Otolaryngol Head Neck Surg. Sep 1997;117(3 Pt 1):8-75.

20. Patel UA, Thakkar KH, Holloway N. *Patient compliance to radiation for advanced head and neck cancer at a tertiary care county hospital.* Laryngoscope. Mar 2008;118(3):428-32.

21. Spector JG**,** Sessions DG**,** Haughey BH**,** et al. *Targeted Molecular Therapy in Head and Neck Squamous Cell Carcinoma*.

22. Posner MR. *Integrating systemic agents into multimodality treatment of locally advanced head and neck cancer.*

23. Radiation Therapy Oncology Group (RTOG)**.** *Age, Stage, and Tumor Location Increase Risk of Late Toxicity After Concurrent Chemoradiation in Patients With Head and Neck Cancer.* Retrospective, nonrandomized, case-control analysis of 3 Oncology Groups.

24. www.national foundation for cancer research.org

25. Radiation Therapy Oncology Group (RTOG). *Phase III randomized study to compare hyperfractionation and two variants of accelerated fractionation to standard fractionation radiotherapy for head and neck squamous cell carcinomas.* Int J Radiat Oncol Biol Phys. 2000; 48(1):7-16 (ISSN: 0360-3016).

26. Acta Oncol.**.***A systematic overview of radiation therapy effects in head and neck cancer.* 2003;42(5-6):443-61

27. Vissink A, Jansma J, Spigkervet F, et al. *Oral sequelae of head and neck radiotherapy.*

28**.** Eisbruch A, Ten Haken RK, Kim HM, et al. *Dose, volume, and function relationships in parotid salivary glands following conformal and intensity-modulated irradiation of head and neck cancer***.** Int J Radiat Oncol Biol Phys**.** Oct 1 1999;45(3):577-87.

29. Thorn JJ, Hansen HS, Spetch L, et al. *Osteoradionecrosis of the jaws: clinical characteristics and relation to field of irradiation.* J Oral Maxillofacial Surg 2000, **58:**1088-1093.Crit Rev Oral Biol Med 2003, **14:**199-212.

30. Strahlenther Onkol. *Side effects of postoperative radiochemotherapy with amifostine versus radiochemotherapy alone in head and neck tumors.* Preliminary results of a prospective randomized trial Nov 1999;175 Suppl 4:18-22..

31. Stell PM . *Survival time in Head and Neck cancer.* Curr Opin Oncol 2009 21:213-218

32. Johansson S, Svesson H, Denekamp J, et al. *Time scale evolution of late radiation injury after postoperative radiotherapy for HNC patient.*Int J. Radiat Oncol Biol Phys 2000:48: 748-50. 32

33. Huguenin PU. Quality of life of HNC patients cured by RT, importance of target volume.Int J Radiat Oncol Biol Phys 2006:26:24-9

36. Purdy J.A. *Three-dimensional conformal radiation, physics, treatment planning and the clinical aspects* in Principles and Practice of Radiation Oncology.

34. Fenet M, Hall J. *Predictive markers of normal tissue reactions.* Cancer raditherapy 2008:12:614-18.

35. Bucholz TA. *Finding of sensitive HNC patients.*Int J Radiat Oncol Biol Phys 1999:45:547-48.

36. Nguyen LN, Ang KK. *Radiotherapy for HNC;alterd fractionation regimens.* Lancent Oncol.2002:11:693-701.

37. Pump J. *A systemic overview of radiation therapy effects in Head and neck cancer.* Acta Oncol 2003: 42(5-6).

38. Maciejewski B, Withers H.R, Taylor J.M, et al**.** *Dose fractionation and regeneration in radiotherapy for cancer of the oral cavity and oropharynx.*Int J Radiat Oncol Biol phys,1989. 16(3):831-43.

39. Mc Bride H and Withers R**.** *Head and neck cancer in* Principles and Practice of Radiation Oncology.

40. Halperin E.C, Perez C.A, Brady L.W. *The discipline of radiation oncology* in Principles and Practice of Radiation Oncology.

41. Purdy J.A. *Three-dimensional conformal radiation, physics, treatment planning and the clinical aspects* in Principles and Practice of Radiation Oncology.

42. David I, Rosenthal MD, Trotti A. *Strategies for managing* Radiation- *Induced mucositis in HNC.*Semin Radiat oncol 2009:19:29-34.

43. Trotti A.*Toxicity in Head and Neck Cancer.* Int J Radiat Oncol Biol Phys, 2000:47(1):1-12.

44. Trotti A. *Toxicity antagonist in head and neck cancer.* Semin Radiat Oncol,1998:8(4):282-91.

45. Kaanders JH, Ang KK. *Early Reactions as Dose Limiting factors in Radiotherapy*. Semin Radiat Oncol, 1994:4(2): 55-67.

46. Fowler JF, Lindstorm MJ. *Loss of local control with Prolongation of Radiotherapy.* Int J Radiat Oncol Biol phys,1992:23(2):457-67.

47. Winn DM, Blot WJ, Austin RS, et al. *Mouthwash use in the risk of oral and pharyngeal cancer.* Cancer Res, 1991:51(11);3044-47.

APPENDECES

Appendix i Consent Form (English)

Conset to participate in study of Head and Neck Cancer patients at ORCI.

Greetings

Madam/ Sir,

My name is Caroline Mrema..... I'm working at ORCI and involved in research on Head and Neck Cancer. Am going to tell you about the study and will ask you to participate in this research. Please be free to ask any question. Purpose of Study:

We are recruiting all HNC patients attending follow up clinic at ORCI during treatment between May and September 2012 and diagnosed between 2010 and 2012. We want to determine the magnitude of radiotherapy side effects among treated HNC patients, their social demographic characteristics,disease profile and the treatment modality given.

Participation:

Those willing to participate will be interviewedon some questions related to the research. Patients will be asked on the type of radiation side effects and physical examination will be done to assess on the morbidity if any that is resulted from HNC treatment.

Confidentiality:

All information collected will be confidential and will be used for the purpose of this study and better care and treatment. No one elseother than the ones involved in this research and health personnel have access in this information.

Benefits and Risks:

All HNC patients that are found to have radiation side effects will be treated for the side effects with no delay. Also you will be able to get medical advice any time you need during the study period by communicating with doctor involvrd in research. The information will assist in improving treatment care and minimizing radiation side effects so as to improve quality of life.

No risk while in this research.

Voluntary participation & Right to withdraw:

Your participation is voluntary and you have the right to discontinue from participation fro participating in our study at any time. However your decision to withdrawal will not affect your right to treatment and care.

Contact Persons :

If you have questions about this study OR in case of any information about your information about your rights as a participant in this study, please contact;

1. The Principal Investigator

Dr. Caroline Mrema, Resident, Clinical Oncology Department

2**. Dr. Khamza Maunda,** Senior lecturer and Supervisor, Clinical oncology Department

3 . **Dr. Julius Mwaiselage**, Coordinator, Clinical Oncology Department.

4**. Chairman of MUHAS IRB**, Prof M. Abood

I .....

Have understood the above information and my questions have been answered to my satisfaction. I agree to take part in this study.

Name of the participant;.....

Signature of the participant.....

Date of signed consent .....

Appendix ii Consent form: Swahili version

Fomu ya ridhaa ya utafiti kwa wagonjwa wenye saratani ya kichwa na shingo wanaokuja kwa matibabu taasisis ya Saratani ya Ocean Road.

Utambulisho.

Habari za saa hizi

Jina langu ni Caroline Mrema ni daktari katika Taasisis ya Saratani ya ocean Road. Ninafanya utafiti kuangalia madhara ya tiba mionzi kwa wagonjwa wenye saratani ya kichwa na shingo hapa Ocean Road. Nitakueleza kuhusu utafiti huu kisha nitakuomba ridhaa yako kushirika katika huu utafiti.

Tafadhali uwe huru kuuliza swali lolote.

Malengo ya Utafiti

Utafiti huu unafanyika kwa wagonjwa wote walioko kwenye tiba ya mionzi ya saratani ya shingo na koo na tunawafatilia kliniki kujua kujua madhara waliyopata kutokana na tiba ya mionzi.

Ushiriki katika Utafiti

Watakaokubali kushiriki katiki utafiti tutawahoji maswali kadhaa kuhusu madhara waliyopata kutokana na tiba ya mionzi. Tutauliza pia ni aina ngapi za matibabu walipata kama ni upasuaji, mionzi na dripu kwa pamoja.

Usiri

Taarifa zote utakazopata/ utakazopata kuhusu wewe ni siri na zinatumika tu kwa ajili ya utafiti huu na huduma bora kwako. Hakuna mtu mwingine zaidi ya wanaohusika na utafiti huu na wahudumu wa afya watakaohudumia atakayesoma au kupata maelezo yako.

Faida

Kupitia utafiti huu washiriki wote watapewa matibabu bila kuchelewa. Pia watapata fursa ya kupta ushauri wa afya zao muda wowote wakati wa utafiti kwa kuwasiliano na daktari mhusika katika utafiti.

Natumaini kuwa taarifa zote zitakazopatikana kutokana na utafiti huu zitasaidia kuboresha huduma na kupunguza madhara yanayotokana na tiba ya mionzi.

Hutapata hasara yoyote kwa kushiriki katika utafiti huu.

Iwapo utakua na swali lolote kuhusu utafiti huu unaweza kuwasiliana

1.Mtafiti Mkuu

Dr. Caroline Mrema, mwanafunzi, Idara ya Clinical Oncology, MUHAS

No. 0713-780029, barua pepe; liasalex@yahoo.com

2. Dr. Khamza Maunda, Senior Lecturer, Idara ya Clinical Oncology, MUHAS

3. Dr. Julius Mwaiselage, Mkuu Idara ya Utafiti wa magonjwa ya Saratani Ocean Road

Mimi.....

Nimeelewa maelezo yaliyoandikw hapo juu na kuridhika na majibu niliyopewa kwa mawasiliano yangu yote. Ninakubali kushiriki katika utafiti huu.

Jina la mshiriki.....

Sahii ya mshiriki.....

Tarehe ya kusaini ridhaa.....

Appendix iii Questionnaire

1. Name…….
2. Registration No……
3. Serial No…….
4. Sex
    i. Male
    ii. Female
5 Age (yrs)……
6. Highest formal education achieved.
    i. none
    ii. primary school
    iii. secondary school
    iv. post secondary
7. Disease stage:
    i. One
    ii. Two
    iii. Three
    iv. Four
    v.Unknown.
8. Radiotherapy dose:
    i. 30 GYs
    ii. 50 GYs
9. Treatment Modalities:
    i.EBRT alone
    ii.EBRT and chemotherapy
10.The determinats of radiation side effects

i.Radioprotector use (Amifostine)

ii.Dose fractionation(Hyprefractionation/ single fraction)

iii.Type of treatment modality(Radiotherapy alone or combined)

iv.Radiosensitizer(Cispatin)

11. Do you have any radiation side effects :

i. Yes

ii. No

12. Which type of radiation side effects do you have:

i. Mucositis(sore throat)

ii.Sore skin

iii. Difficult in swallowing/ feeding difficulties

iv.Xerostomia