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COBALT-60 RADIATION BEAM VERIFICATION IN NASOPHARYNGEAL CARCINOMA: A KENYAN EXPERIENCE

by

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DECLARATION

I, Richard Malakwen Kikwai, declare that the contents of this thesis represent my own unaided work, and that the thesis has not previously been submitted for academic examination towards any qualification. Furthermore, it represents my own opinions and not necessarily those of the Cape Peninsula University of Technology.

Signed **Date**

ABSTRACT

Background and purpose

The primary aim of this study was to analyse the accuracy and reproducibility of radiation treatment to patients with nasopharyngeal carcinoma at the only tertiary teaching and referral hospital in Kenya. The secondary objective was to review literature on quality assurance procedures that would result to provision of quality radiation treatment to this group of patients.

Materials and method

During the period May 2011 to March 2012, 35 patients with head and neck cancer comprising of 27 patients with nasopharyngeal carcinoma, 7 with paranasal sinus carcinoma and 1 with lymphoma falling within the enrolment criteria were treated using Equinox cobalt-60 unit with the same beam arrangement and were studied prospectively. Radical radiotherapy was delivered using conventional 2D technique in a routine dose of 60-66Gy to the primary and 50Gy to lymph nodes with additional dose to residual neck nodes. During the period of their treatment, a lateral portal image was taken once weekly. Four film image pairs were obtained per patient with each patient positioned and immobilised in an individualised Orfit thermoplastic mask and a head and neck support. The 4 portal images were compared to a corresponding simulator film taken during simulation planning. Deviations from the varied bony landmarks were measured on the portal images and simulator image from the centre of the radiation beam. These measurements were used to calculate systematic and random errors.

Results

The overall mean in beam alignment indicated systematic and random errors to be 4.4mm and 1.08mm respectively. Although the means are within the reported range by other studies, the difference between the simulator and the portal images of individual patients varied between no difference (0.0mm) as the minimum and 11mm as the maximum with the lower 95% confidence level (CL) of mean being 3.23mm, the upper 95% CL of mean being 5.58mm. Further, 37.5% (n=12) of the patient measurements were within 2mm, 56.25% (n=18) were within 4mm and 43.75% (n=14) indicated a difference greater than 4mm.

Conclusion

This prospective study has shown the probable range of systematic and random errors that occur in beam alignment during the course of radiation treatment to this group of patients at the study site. To ensure that radiation treatment is delivered as planned, portal imaging needs to be implemented on a routine basis in order to monitor, document and allow for mechanisms to correct observed errors through portal imaging QA and QC. The results of this study have shown the disparity of the delivered treatment from the planned, as a result of beam alignment errors, which indicate that certain measures need to be implemented at the study site in order to limit these errors to within international recommendation.

This study has confirmed that the observed variations were considerably outside the limits of international standards in terms of systematic errors. These errors compromise the quality of treatments delivered at the study site. Recommendations for improved quality have been provided and the researcher is of the view that if the recommendations are adopted, the observed errors would be minimized to within the recommended 2mm.

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GLOSSARY

Terms/Acronyms/Abbreviations	Definitions/Explanation
NCRP:	National Council on Radiation Protection and Measurements
IPEMB:	Institute of Physics Engineering in Medicine and Biology
RCR:	The Royal College of Radiologists
WHO:	World Health Organisation
IAEA:	International Atomic Energy Agency
ICRU:	International Commission on Radiation Units and Measurements
CAPCA:	Canadian Association of Provincial Cancer Agencies
AAPM:	American Association of Physicists in Medicine
KEMRI:	Kenya Medical Research Institute
KNH:	Kenyatta National Hospital
Conformal Radiation Therapy:	A radiation therapy technique that uses multiple radiation beams that are each custom-shaped to conform the high dose of radiation to the tumour while sparing the normal tissue. It is also known as 3-D or conformal radiation therapy
Conventional Radiation Therapy:	Radiation therapy based on relatively broad beams with simple, standard beam shapes and a limited number of gantry angles
Heterogeneity:	Refers to the condition when the volume of the patient or a phantom consists of different composition and density
(IMRT):	(Intensity Modulated Radiation Therapy) An advance method of conformal radiation therapy in which the intensity within a radiation beam is modulated during treatment to spare more adjoining normal tissue than is spared during conventional or 3-D conformal radiation
Inverse Treatment Planning:	An automated process, which begins with a desired dose distribution and comes up with a set of optimized beam parameters that make it possible to deliver a dose distribution similar to the desired one
Multi-leaf Collimator (MLC):	A special type of collimator which can define irregularly

	shaped radiation fields. An MLC has narrow, interlaced metal blocks (leaves) that can be independently driven in or out of the beam to regulate the amount of radiation passing through
RTT:	Refers to Radiation Therapy Technologist also referred to as therapy radiographer or radiotherapy radiographer in some countries
QA:	Refers to quality assurance in radiation therapy. It is all those procedures that ensure consistency of the medical prescription and the safe fulfilment of the dose to the normal tissue, minimal exposure of personnel, and adequate patient monitoring aimed at determining the end result of the treatment.
QC:	Refers to quality control in radiation therapy. It is the measures taken to control, restore, maintain and or improve the quality of radiation treatment. Aimed at monitoring and eliminating causes of unsatisfactory performance.

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Chapter One

1.1 Introduction to cancer

Cancer is a disease that results from failure of the mechanisms that regulate normal cell growth and cell death leading to uncontrollable proliferation of cells, destruction of neighbouring tissues and spread of the disease to other parts of the body (IAEA, 2003). However, several authors (IAEA, 2003: Jemal, Bray, Center et al, 2011: Parkin, Bray, Ferlay et al, 2005) indicate that it is possible to significantly reduce the effects of cancer on the society if effective actions are put in place to control risk factors associated with cancer, introduce measures for early detection and offer good care to those affected.

1.2 Global Cancer Incidence

The World Health Organisation (WHO, 2008a) has reported cancer to be a leading cause of death globally and estimates that 7.6 million people died of cancer in 2005 and 84 million people will die in the next 10 years. Cancer is currently the cause of 12 per cent of all deaths worldwide (WHO, 2002). Unfortunately, more than 70 per cent of all cancer deaths occur in countries where resources available for prevention, diagnosis and treatment are limited (WHO, 2008a). Another WHO report (WHO, 2002) indicates that there are 20 million people currently living with cancer in the world. The estimated number of new cases each year is expected to rise from 10 million in the year 2000 to 20 million by the year 2020, of which the majority 70 per cent will occur in less developed parts of the world with less than 5 per cent of the resources for cancer control (Sikora, 1999:24-31). Nasopharyngeal cancer is the most common head and neck cancer and considered as one of the rare cancers ranking as the 24^{th} most frequently diagnosed cancer form worldwide (Jemal et al 2011). Cancer of the nasopharynx makes up approximately 14.8% of the total number of reported cases of cancer in Kenya and constituting the largest proportion of cases in males (Wanja, 2010).

1.3 Cancer Incidence in Africa

Statistics for the African continent are reported to have a large measure of inaccuracy due to inadequacy in population based cancer registries (WHO, 2008b:16-17). It is estimated that there were 871 000 incidences of cancer in 2008 (353 000 in men and 518 000 in women) with a total of 518 000 (252 000 in men and 266 000 in women) deaths from cancer. The cancer incidence in Africa varies from the global incidence and this could be attributed to causative factors which are different from region to region or country to country. NPC accounts for 5.1 per cent of all deaths in Africa (WHO, 2002) with elevated rates reported in southern Africa, and Northern Africa particularly in Tunisia and Algeria (Jemal et al, 2011). A recent report by Barton, Frommer, & Shafiq (2006) gives the yearly breakdown of incidence of NPC in Africa to be 2640 in East Africa, 388 in Central Africa, 2816 in Northern Africa, 343 in Southern Africa, 1964 in Western Africa and the total in all Africa to be 8151.

1.4 Cancer incidence in Kenya

The global statistics, as shown in section 1.1, indicate an upward trend in the incidence of cancer. In Kenya, a controlled policy document released in 2011 and available at the study site, indicates that cancer causes 7% of total national mortality every year and ranks third as a cause of death after infectious diseases and cardiovascular diseases. Although population based data does not exist in the country, it is estimated that the annual incidence of cancer is about 28,000 new cases and the annual mortality to be over 22,000 with over 60% of those affected falling below the age of 70 years (National cancer Control Strategy, 2011-2016). Unpublished cancer data of 2008 reported by the department of medical records at the study site in 2010 (Department of medical records, 2010) indicate that cancer killed approximately 18,000 people in Kenya in 2005. Kenya does not have a national cancer registry and the only available information is from the main hospitals in Nairobi dating back to year 2000 (Wanja, 2010). This may not be representative of the incidence in the country because many patients may not make it to the point of treatment in the city due to financial constraints and the booking system in an already congested facility.

The most current information regarding cancer incidence in Kenya is available in unpublished institutional documentation released in 2010 by Department of medical records at the study site. It indicates that new cases of cancer increased by 29 per cent, from 9755 cases in 2004 to 11129 cases in 2008. The old cases morbidity trend recorded a 14 per cent increase from 1499 cases in 2004 to 1927 cases in 2008. Generally, cancer of the cervix had the highest incidence followed by that of cancer of the breast while cancer of the nasopharynx ranked third. NPC makes up the largest proportion of reported cases of cancer in Kenya, males constituting about 14.8% of the total number of reported cases (Wanja, 2010). Unfortunately, these patients do not have access to immediate radiation therapy services due to inadequate availability of treatment facilities in Kenya, typical of developing countries as evidenced by several authors (IAEA, 2008; Salminen et al., 2005; Barton et al., 2006; Levin et al., 1999).

1.5 Rationale

Nasopharyngeal carcinoma (NPC) is one of the most challenging tumours in the delivery of radiation treatment due to its close proximity to critical organs and radiosensitive tissues (Wei & Sham, 2005). Typically, in the treatment of nasopharyngeal carcinoma, large parallel-opposed lateral portals are used to encompass macroscopic disease and sites of nodal metastases. With this technique, parotid glands, temporal lobe, spinal cord and brainstem are inevitably included in the treatment volume leading to complete xerostomia, risk of temporal lobe necrosis and myelopathy (Razak et al., 2010; Wei & Sham, 2005).

Although NPC is not a common malignancy, it affects the most visible area of the body, and may have profound impact on the most fundamental activities of daily living such as speech, breathing, kissing, eating and drinking (Mould & Tai, 2002; Wells, 1998). Radiotherapy plays a key role in the treatment of head and neck cancer (Mould & Tai, 2002) but when side-effects are superimposed on existing functional difficulties, morbidity is significant (Mould & Tai, 2002; Wells, 1998). Therefore, radiotherapy requires accuracy and reproducibility of radiation dose to the target volume in order to maximise the dose to the target volume while minimising dose and toxicity to critical normal structures (Naiyanet et al, 2007). In order to confirm that the radiation treatment

is directed to the tumour volume as planned, it is important to have quality control for geometric accuracy of radiation beam alignment by portal imaging.

As an important tool in the confirmation and verification process, radiation therapy portal imaging entails producing images using the radiation treatment cobalt 60 unit or linear accelerator to form an image of the area being irradiated (Langmack, 2001). Portal imaging is the most common method available for measuring and documenting the extent of geometric treatment accuracy and reproducibility (Thwaites et al., 2005).

In order to apply portal imaging, local QC protocols have to be established stating the frequency of portal imaging, the criteria for acceptability of observed set-up deviations, and the responsibility for making decisions for changing the patient position (Hurkmans et al., 2001). Careful analysis of the results of a portal imaging programme can trace several errors such as the imperfect alignment of lasers or differences in couch sagging during CT scanning and actual patient treatment (Thwaites et al., 2005). Portal imaging may also lead to various strategies to improve treatment accuracy even further in a department, for instance with respect to patient immobilisation and patient positioning by the RTTs (Hurkmans et al., 2001). As this study concerns set-up (beam alignment) verification of radiation treatment, dose verification is beyond the scope of this study.

1.6 Research focus

This study was conducted from the basis of the absence of QC procedures on portal imaging at the study site. The quality control of radiation treatment to patients with head and neck cancer is documented by the Royal College of Radiologists (2008) as a standard QA practice of verifying the accuracy and reproducibility of radiation treatment to patients. Portal imaging, an important component of radiation therapy with the primary role of detecting treatment delivery errors, is indicated by several authors (IAEA, 2008; Thwaites et al.,2005; Suter et al.,2000; Van Dyk, 1999) as a procedure which should be undertaken on a weekly basis. The absence of this practice at the study site was seen as a problem by the researcher. This study therefore evaluated a group of patients at the study site using portal imaging in order to understand how the practice compare with

international recommendations in terms of accuracy and reproducibility of radiation treatment to patients with cancer in the head and neck region.

1.7 Research aim

The aim of this study was to prospectively analyze the accuracy and reproducibility of the radiation treatment of patients undergoing radiation therapy with curative intent for nasopharyngeal cancers on a cobalt-60 radiation therapy unit at an academic hospital in Kenya.

Through an interpretation of the findings, it was anticipated that the outcome of the study would provide a basis for internal audit of the accuracy of radiation treatments to patients undergoing treatment for head and neck cancers at the study site. It is postulated by the researcher that the study may provide input into improvement of departmental protocol that ensures accurate and reproducible radiation therapy to patients with head and neck cancer, hence help with upgrading and improvement of radiation therapy service in Kenya in line with current IAEA recommendations for quality provision of radiotherapy services (IAEA, 2008). The study site presents the radiation treatment experience of a department that is representative of the radiation therapy centres in East Africa and many countries in the rest of Africa with limited resources for radiation treatment.

1.8 Research question

The research question that was addressed in this study was ‘What is the accuracy and reproducibility of the treatment to patients with nasopharyngeal cancer on Equinox Cobalt-60 unit?’

Three further sub-questions were:

1. How accurate is the treatment field placement on the radiation therapy unit?
2. How reproducible is the treatment set-up during the period of radiation therapy?
3. What are the recommended QC measures that ensure radiation therapy is accurate and reproducible?

1.9 Research objectives

The objectives explored in the study in order to realize the research aim and the answer to the research question were:

1. To determine the accuracy of daily radiation therapy to patients undergoing radical treatment for nasopharyngeal carcinoma through the analysis of verification port films taken on Equinox cobalt-60 unit in relation to the simulation film

2. To evaluate the reproducibility of daily treatment to patients during the period of their radiation treatment

3. To identify the QC measures that ensure the radiation treatment is accurate and reproducible

1.10 Nasopharyngeal cancer (NPC)

1.10.1 Incidence

Globally, NPC is reported by Jemal et al (2011) to be relatively uncommon giving an estimate of 84,400 incident cases and 51,600 deaths in 2008, representing about 0.7% of the global cancer burden. The figures given by Jemal et al (2011) compare closely to those given by Razak, Sui, Liu et al (2010) and similar to those given by Ferlay, Shin, Bray et al (2011) of 80,000 new cases and 50,000 deaths annually. In Europe and North America the incidence are reported as below 1 in 100,000 (Spano et al., 2003). High incidences have however been reported in Southern China and in migrant populations of Southern Chinese origin (Spano, et al 2003). In Southern China, rates as high as 10-150 per 100,000 populations has been reported per year (Her, 2001) and closely compare with the figures by Chan et al (2002) of 15 -50 per 100 000 and being more common among men. NPC is reported by Jemal et al (2011) to be more frequent in males than females in both developing and developed world, with incidence rates commonly 2 to 3 times higher in males in higher resource countries, with male to female ratios considered higher in developing countries. NPC in higher resource settings is more associated with lifestyle related risk factors; the decreasing smoking prevalence among US males, for example,

has been postulated as a contributor to the overall decline in NPC incidence (Hsu et al., 2003). Other populations where NPC is relatively frequent include the Inuit populations of Alaska, Greenland, and North Canada, as well as Chinese and Filipinos living in the United States (Curado et al, 2007; Parkin et al, 2003; Yu, 2006).

1.10.2 Risk factors

Progress has been made in defining NPC carcinogenic evolution and understanding its association with Epstein-Barr virus, environmental factors, and diet (Spano, et al 2003). Infection with Epstein - Barr virus (EBV) is important in etiology because it is said to be present in all NPC tumour cells and thus can be used as a diagnostic indicator (Parkin et al 2005). In addition, EBV levels have been reported to correlate with response, (Lo et al., 1999a; Lo et al.,1999b; Lo et al., 2000) and they may predict disease recurrence (Lo et al, 1999b) suggesting that it may be an independent indicator of prognosis (Lin et al., 2004). Certain foods have been documented as risk factors associated with NPC, a number of studies (Hildesheim & Levin, 1993; Klein, 2002; Chan et al., 2002; Spano et al, 2003) have reported increased risk factors associated with foods eaten within areas of high incidence which include salt-cured fish and meat, consumption of other preserved foods and hot spices and relate these foods to high content of nitroso compounds and volatile nitrosamines, considered carcinogenic. An example is in North Africa where early exposure in life to preserved spiced meat, basic stewing preparations and hot pimento paste taken with bread have been associated with higher incidence of NPC (Jeannel et al., 1990).

The only study found on NPC at the study site, with links to risk factors, is one done in a ten-year period 1961-1970 by Clifford (1972) in which a study on 434 patients with NPC was done on all patients admitted to the study site. Clifford (1972) then noted a male preponderance of 2.65:1 in the study group with the highest age-specific occurring in 50-54 years and notes that the highest rates occurred in those tribes living in the higher and subsequently colder areas of the country, irrespective of ethnic origin. Clifford (1972) associated the occurrence of NPC with smoke from wood fire in poorly ventilated, circular huts, where wood fire for cooking and heating burns for much of the day. The

high concentration of smoke within the huts, Clifford (1972) notes, deposited soot over the entire interior of the roof. The author (Clifford, 1972) indicated that the soot samples collected from the huts of 30 patients with NPC and analyzed at the Sloan-Kettering Institute in New York indicated high values of carcinogenic hydrocarbons as a result of the amount of benzypyrene and benzanthracene in the air in the interior of the huts. In this study, it is postulated that the information provided by Clifford then, could still be a major causative factor for the current study group because wood fire is still the most common source of fuel, and thus this study group present with an environmental exposure to carcinogens as the main causative factor in addition to EBV.

1.10.3 Presentation of NPC

Although a nose bleed, stuffy nose with bloody discharge, or otitis media are given as an indication of early clinical symptoms of NPC (Vokes et al., 1997), NPC exhibits few early warning signs, the tumour may initially grow unnoticed and spread locally to the adjacent areas in the throat or invade the base of skull causing neurologic symptoms which present as cranial nerve paralysis (Spano et al., 2003). This probably explains the reason why the majority (75-90%) of newly diagnosed patients are reported to have loco-regional advanced disease, commonly with cervical nodal metastases (Razak et al., 2010; Spano, et al., 2003). Other symptoms are pointed out by Chan et al. (2002) to be difficulty in breathing, lump in the neck, and damage to nerves in the head and neck. In addition Spano et al. (2003) indicate other symptoms to be diplopia (bulging of eye(s) due to nerve invasion) and pain. Chan et al. (2002) indicate that once the diagnosis is suspected on clinical grounds, that histologic confirmation is mandatory in order to institute appropriate treatment strategy.

1.10.4 Histopathological classification

Pathology has an important impact on outcome and three subtypes of NPC are recognised in the World Health Organisation (WHO, 1978).

- Type 1: Squamous cell carcinoma, typically found in the older adult population
- Type 2: Non-keratinizing carcinoma

- Type 3: Undifferentiated carcinoma being the most common

Spano et al., (2003) use the above histopathological classification and gives other histological forms of NPC to be lymphomas or plasmocytomas.

1.10.5 Staging of NPC

Treatment options are decided upon by a radiation oncologist following diagnostic assessment of the head and neck area, which involves classification of the cancer according to the International Union Against Cancer (UICC) and American Joint Committee on Cancer (AJCC) TNM staging system which is the most frequently used system (UICC, 1997; Spano et al., 2003). In this TNM system, T stands for tumour, N for nodal involvement and M for metastasis (UICC, 1997; Spano et al., 2003; Chan et al., 2002). In order to accurately stage the tumour, pathologists are guided by the TNM factors to determine how large the primary tumour is and its location; if the tumour has spread to the lymph nodes; and if tumour has spread to other parts of the body (Spano et al., 2003; Chan et al., 2002). Understanding TNM is important for it provides characterization of the tumour which in turn has provided prognostic factors for overall survival and predictive information allowing for the optimal treatment sequence (Spano et al., 2003). Although NPC is radiosensitive and chemosensitive when compared with other head and neck cancers, advanced stage NPC is associated with the high rate of treatment failure, with a high risk of local recurrence and distant metastases (Spano et al., 2003) which thus suggest prompt and carefully planned radiation therapy sequencing and delivery.

Table 1.1 TNM staging of NPC according to 5th UICC, 1997

T Stage	
T1	Tumour limited to one subsite of nasopharynx
T2	Tumour invades more than one subsite of nasopharynx
T3	Tumour invades nasal cavity and/or oropharynx
T4	Tumour invades skull and/or cranial nerve(s)
Regional lymph nodes (N)	
NX	Regional lymph nodes cannot be assessed
NO	No regional lymph-node metastasis
N1	Metastasis in a single ipsilateral lymph node, ≤ 3 cm in greatest dimension
N2	Metastasis in a single ipsilateral lymph node, >3 cm but ≤ 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none >6 cm in greatest dimension; or in bilateral or contralateral lymph nodes, none >6 cm in greatest dimension
N2a	Metastasis in a single ipsilateral lymph node >3 cm but ≤ 6 cm in greatest dimension
N2b	Metastasis in multiple ipsilateral lymph nodes, none >6 cm in greatest dimension
N2c	Metastasis in bilateral or contralateral lymph nodes, none >6 cm in greatest dimension
N3	Metastasis in a lymph node >6 cm in greatest dimension
Distant metastasis (M)	
Mx	Presence of distant metastasis cannot be assessed
Mo	No distant metastasis
M1	Distant metastasis

Table 1.2 NPC Stage grouping

Stage 0	**Tis**	**No**	**Mo**
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage IV	T4	N0	M0
	T4	N1	M0
	Any T	N2	M0
	Any T	N3	M0
	Any T	Any N	M1

1.10.6 Prognostic factors

For the vast majority of patients with NPC, the cure rate with primary radiotherapy is given to be approximately 65% to 100% for T1 tumours, and falls to 5% to 40 % for T4 tumours (Torgil, 1996), and this compares closely to a more recent report by Razak et al., (2010) which gives a 3 year disease-free and overall survival rate to be of 70% and 80% respectively. Further reports indicate 5 year survival with adequate radiotherapy to be 30% to 80% (Chatani et al., 1993; Bailet et al., 1992) with a 10 year survival reported at 20% to 60% (Lee et al., 1992; Johansen et al., 1992). Boost technique is reported to yield better results either as intracavitary treatment or using external 'cone down' technique with doses up to 120Gy-150Gy (Yan et al., 1989; Yan et al., 1990). Presentation with clinical lymph nodes implies the disease has spread beyond the primary site with factors associated with a poor prognosis being skull base invovement, extent of the primary tumour and cranial nerve involvement (Razack et al., 2010). A failure rate of 15-19% with distant metastases have been reported after primary radiotherapy with temporal lobe necrosis and xerostamia recognised as late side effects of radiation therapy for NPC (Razak et al., 2010).

1.11 Development in radiation therapy of NPC

Treatment of NPC using external beam radiotherapy is documented by Mould and Tai (2002) to have evolved during the 20th century and still evolving. Together with the advancement of radiation treatment, diagnosis of NPC has also improved with the availability of CT and MRI (Mould & Tai, 2002). A brief description of the technological advancement in the radiation treatment of NPC is given under historical, transitional and modern era. Understanding the technological advances is important for together with early diagnosis, adequate radiation dose to the primary with boost to the bulky disease, and better delineation of tumour with current imaging technology, improved outcome has been reported (Mould & Tai, 2002).

1.11.1 Historical era

Since the discovery of x-rays in 1895 by Roentgen, radiation has been put to use in medical imaging and in radiation therapy of NPC with the first proven successful x-ray treatment of histologically verified cancer in 1896 and concerned treatment of an 89 year old patient (Mould & Tai, 2002). It is postulated that the NPC patient provided the first evidence of relief of pain as an outcome of x-ray treatment and during the period 1900-1920, Mould and Tai (2002) indicate that there was no mention of NPC in textbooks. This is not surprising for NPC was rare, only 13 cases were found to have been reported in medical literature before the 20th century (Jackson, 1901; McCarty & Million, 1994). Another possible reason for no mention of radiation treatment for NPC during this period is that x-ray tubes had not been developed to provide treatment and thus would have extremely poor depth dose characteristics that discouraged its use (Mould & Tai, 2002).

In the period 1921 to 1950 200kV x-rays at short source to skin distance is reported by Mould and Tai (2002) to have been in use in the treatment of NPC. These units are referred to as orthovoltage units and generate x-rays with the energy range of 150-500 kV and such x-ray beams exhibit fast dose fall-off with depth in the patients' body thus beneficial for treating superficial tumours. The use of x-rays at these energy range was reported to yield a 5 year survival rate of 11.4% in 70 cases (McCarty & Million, 1994) and compares closely to those reported by New and Stevenson (1943) of 15.6% 5 year survival of 32 patients with radiation dose delivered being 500 roentgen. Additional dose

was limited by tolerance of the skin (Mould & Tai, 2002). The advent of cobalt-60 teletherapy units after 1950 significantly improved prognosis of NPC patients.

1.11.2 Transitional era

Widespread introduction of cobalt-60, as indicated by Mould and Tai (2002), occurred during this period and marked the start of megavoltage radiation treatment of NPC with doses to primary being 5400rad in two phase field arrangement with cone down of second field to avoid the spinal cord and 4800rad to the neck field. These units were put to use with brachytherapy (Iridium-192 at times used in combination with external beam therapy (EBRT) and is reported to have yielded a 5 year overall survival of 42% (Mould & Tai, 2002). The use of Cobalt-60 EBRT and the administration of brachytherapy in the treatment of NPC yielded improved results due to the advanced technology which allowed dose escalation (Mould & Tai, 2002). However, cobalt-60 units provide relatively high energy megavoltage gamma rays that penetrate deeper into the patients but with some skin sparing effects which enable delivery of sufficient curative dose to deep-seated tumours without exceeding the skin dose.

Some authors have indicated that advanced NPC require doses higher than achievable only from a cobalt-60 treatment unit due to residual neck nodes. Cobalt-60 has therefore been used with linear accelerators. The electron capability from a linear accelerator has enabled the use of both equipment to enhance dose escalation while sparing the spinal cord.

1.11.3 Current practice

Effective radiation treatment to NPC is by conformal radiation therapy (3DCRT & IMRT), to achieve this, correct tumour localisation is essential and therefore tumour volumes, treatment volumes and organs at risk need to be defined using a standard convention as provided by the ICRU report 50 (1993) and the ICRU report 62 (1999). CT is the main imaging modality and used as a standard to provide high quality images which ensure reliable tumour volume delineation. This has in turn enabled delivery of higher treatment dose to smaller target volumes which then result in less normal tissue

damage an increased overall survival. Relying on a clear convention for defining tumour volume, use of accurate CT image sets, advanced beam collimation techniques and accurate dose calculation computer software are the essentials in the provision of conformal radiation therapy to NPC.

Conformal radiation therapy is the primary modality of choice due to the radiosensitivity of NPC, surgical intervention is limited in early stage disease due to the complex anatomic location of the disease (Spano et al., 2003; Chan et al., 2002). However, surgery has been used to treat recurrent NPC or to remove lymph nodes in the neck (Spano et al., 2003). Chemotherapy given in conjunction with radiation therapy is reported to significantly improve survival rate of patients (Spano et al., 2003; Vokes et al., 1997). Cisplatin and 5-FU is reported to be the most popularly used agents and considered as first line chemotherapy drugs for metastatic NPC (Spano et al., 2003; Chan et al., 2002; Vokes et al., 1997). Several Phase III clinical trials have proved that concurrent chemoradiation therapy improves the overall survival from 50% to 70% in locally advanced nasopharyngeal carcinoma (Lin et al., 2003; Kwong et al., 2004; Al-Saraff et al., 1998).

Cisplatin has been reported as the most active agent against NPC and thus commonly used as concurrent chemo-radiation therapy because its toxicities do not overlap with those of radiation. Myelosuppression is uncommon; therefore optimal doses can be delivered. Al-Saraff et al. (1998) reported on 27 patients treated with concurrent chemo-radiation therapy using cisplatin 100mg/m^2 every 3 weeks for 3 courses. The side effects were tolerable with no interruption of radiotherapy, and the disease free survival, overall survival, and incidence of distance metastases were better in this group when comparison was done with historical controls (Al-Saraff et al., 1998).

1.12 Radiation treatment equipment

1.12.1 African context

Radiation treatment is said to benefit fifty per cent of all patients diagnosed with cancer treated either curatively or palliatively. However the complexity and cost of treatment units has been indicated to be the major factor in their scarcity in developing countries (IAEA, 2008). The geographic disparities in the burden of NPC in relation to resources are noteworthy, with an estimate 92% of new cases, as reported by Jemal et al. (2011), to be occurring within economically developing countries. It is estimated that approximately 3300 external beam radiation treatment machines are in use in these countries, which falls below the recommended estimate of 5000 radiation therapy units considered adequate for the treatment of cancer incidence in these countries (IAEA, 2008). This is based on a rate of approximately one machine for every five hundred new cases of cancer, but out of 56 countries in Africa, only 22 are known to have megavoltage therapy units with the population served by each machine ranging from 0.6 million to 70 million (Levin et al., 1999). Levin et al. (1999), in their report, identified 155 megavoltage machines in Africa out of which 79, (51%) were in only four countries, with Egypt and South Africa being the leading countries in the use of Linear accelerator megavoltage units while the rest mainly use cobalt-6o megavoltage units. This concurs with a report by Bese, Munshi & Budr Ukkar et al. (2008) that the current supply of megavoltage radiation therapy machines (cobalt-60 or linear accelerator) is only 18% of the estimated needs in some parts of developing countries. Although the numbers of radiation treatment units continue to increase in developing countries, there is still a substantial undertaking needed in the coming years to satisfy the needs of the patients with cancer (IAEA, 2008).

Cobalt-60 radiation treatment units are recommended for departments in developing countries for they are simple technologically and provide effective treatment (WHO, 1995). In relation to the more recent and complex linear accelerator radiation treatment units, cobalt-60 units are relatively inexpensive to buy, easy to maintain and can provide adequate radiation therapy for most patients. The World Health Organization reported in

1995 that the majority of treatable cancers in developing countries could be comfortably treated on cobalt-60 (WHO, 1995).

1.12.2 Kenyan context

In Kenya, despite the fact that cancers are on the increase (section 1.3 & 1.4), a controlled Policy document (National Cancer Control Strategy, 2011-2016) explains that the health system in the country has traditionally concentrated on the prevention and control of communicable diseases. As a result, health and development plans have not adequately invested in the prevention and control of cancer and other noncommunicable diseases (National Cancer Control Strategy, 2011-2016). Although the initial investment in establishing radiation therapy equipment is significant, the long life of radiation therapy equipment (20-30 years) means that the cost per patient treatment can be modest (Bese et al., 2008).

Unfortunately, there is little incentive to encourage programmes for early detection of cancer when facilities for treating it are inadequate (WHO, 2003). It has been demonstrated that radiotherapy is cost-effective for cure or palliation, therefore, strategies for developing services are needed urgently to benefit many patients who currently are unable to access radiation treatment (Bese et al., 2008).

According to the regional cancer registry at KEMRI, about 80% of reported cases of cancer are diagnosed at advanced stages, when very little can be achieved in terms of curative treatment (National Cancer Control Strategy, 2011-2016). This is largely due to the low awareness of cancer signs and symptoms, inadequate screening services, inadequate diagnostic facilities and poorly structured referral facilities. The country has few cancer specialists who are concentrated in a few health facilities in the city of Nairobi. This makes it difficult for a great majority of the population to access cancer treatment services resulting in long waiting times causing some previously curable tumours to progress to incurable stages. The reason for this sad situation is that cancer treatment infrastructure in Kenya is inadequate and some cancer management options are

not readily available necessitating some Kenyans to seek cancer treatment abroad (National Cancer Control Strategy, 2011-2016).

The patient numbers at the study site (section 1.4) and the inadequate radiation treatment units (section 1.11) suggest that additional treatment units are needed in order to meet their radiotherapy needs. At the outset of this proposed study, the treatment infrastructure at this study site requires upgrading. This concurs with Ravichandran (2009) that the scenarios of radiation oncology infrastructure in most developing countries remain discouraging and that only a few sites have the following radiotherapy planning facilities: localisation capability, 3D imaging and planning software, and radiation laboratory (mould room) facilities. IAEA (2008) indicate that in order to operate a radiotherapy centre effectively, efficiently and safely, it is necessary to have appropriate equipment, dedicated and properly trained staff, and sensible procedures geared to the economic situation in the region. This report also gives the essential equipment and staffing for a basic radiotherapy setting which suggest that more needs to be done at the study site to meet the radiotherapy needs of the patients with cancer. Barton, Frommer and Shafiq (2006) indicate that in the year 2000, Kenya had an estimated number of new cases of cancer of 27,337 in a population of 34.7 million and documented that the estimated demand for megavoltage machines were 36 at the time. The current population might calculate to a higher demand for these megavoltage equipment. The late stage presentation of cancers, typical of developing countries as documented by Barton et al. (2006), as at the study site require radiation therapy usage in 100% of new cases.

1.13 The study site

The study site is the only state run radiation therapy department at the largest national referral and teaching hospital in Kenya with the capacity to provide radiation therapy services to patients with cancer. The department was started in 1968 and currently has two cobalt-60 isocentric treatment units. In addition, one conventional Simulator, one high dose rate (HDR) brachthyerapy unit, one low dose rate (LDR) brachytherapy unit and a treatment planning system (TPS) are available, though currently non functional apart from the simulator.

The two cobalt-60 units are the only treatment machines for external beam radiation therapy at the centre and serving the entire country, the units therefore are put to use for treatment for a period of 13 to 15 hours daily. The weekly treatment schedules are from Monday to Friday treating an average of 80 patients daily on each unit. One of the units has been in use for approximately 17 years while the second unit, which was used for this study, was commissioned in April 2011.

1.13.1 Treatment technique at the study site

Treatment of radical intent for head and neck cancers at the study site is by conventional technique using two lateral beam portals and an anterior lower neck beam portal. The dose is however based on calculations along central axis because of lack of facilities for computer planning. External beam treatment in this protocol involves administration of 2Gy daily for 5 days per week over six weeks. This is applicable for treatment of lateral beam portals but the portals are adjusted off cord at 44Gy. This is the first part of treatment and is referred to as 'plan 1'. Treatment portals are reduced to cover the primary tumour site and exempt spinal cord from the radiation field after completion of plan 1. The reduced primary treatment volume is treated with the same dose administration schedule to a total dose of 60Gy under the next plan referred to as 'plan 2'. Lower neck anterior beam portal is treated with the same dose fractionation to a total dose of 50Gy with midline shielding of the cord. Shielding is achieved by use of standard lead-blocks on a Perspex plate which slides into collimator slot of the cobalt-60 radiation therapy unit. The treatment set-up parameters and shielding guidelines are based on the simulation printouts and documentation. During the period of their radiation therapy, patients were routinely reviewed once weekly to monitor the progress of treatment and related side effects. Weekly cisplatin administration was found to be common in the study group. Treatment verification check film is not a routine procedure.

1.14 Overview of thesis

The current chapter introduced the context and problem surrounding this study. It provided the motivation and rationale for the study and explained the research question and sub questions. A brief of the content of the chapters in this thesis is given below.

Chapter 2 Literature review

This chapter reviews literature related to this study. It provides a theoretical framework for the empirical research component in this study which measured the accuracy and reproducibility of a conventional 2D radiation treatment technique at the study site. It also gives an interpretation of the past and current literature on the topic of radiation therapy beam alignment verification of patients with nasopharyngeal cancer on cobalt 60 and digital megavoltage units.

Chapter 3 Research methodology

Chapter three explains the research design formulated in order to carry out data collection which would enable analysis as planned for the study. A pilot study was used to provide information that allowed for a method used in the collection of data. Also, details of site and participant selection are provided. The choice of quantitative method is explained, data collection, analysis method is described, ethical considerations given, validity and reliability are also addressed.

Chapter 4 Results

In this chapter, the results of the study are presented using appropriate methods which give meaning to the collected and analysed data. The results were categorized as followed: patient characteristics, histopathological presentation to include tumour staging and the portal film study.

Chapter 5 Discussion, limitations, conclusion and recommendations

This is a final chapter which discuss the findings, limitations, recommendations and conclusion. It also provides possible areas for future research in this study and the contribution of this research in radiation therapy to patients with nasopharyngeal carcinoma.

Chapter Two

Literature review

2.1 Introduction

Chapter one introduced the context and problem surrounding this research. It provided the motivation and rationale for the study and explains the research question and sub questions. Chapter 2 provides a theoretical framework for the empirical research component in this study which measured the accuracy and reproducibility of a conventional 2D radiation treatment technique at the study site. It also gives an interpretation of the past and current literature on the topic of radiation therapy verification of patients with head and neck cancer on cobalt 60 and digital megavoltage units. It further discusses the portal imaging as a necessary quality assurance tool in the current radiation treatment techniques for head and neck cancer, such as 3DCRT, IMRT, and IGRT.

2.2 Requirements for radiation therapy in Nasopharyngeal cancer

Radiotherapy for nasopharyngeal cancer requires accuracy and reproducibility of radiation dose to the target volume due to the close proximity of many critical organs (Naiyanet, et al. 2007). During the EBRT, high energy radiation from a cobalt unit or linear accelerator (approximately 6-8MV x-rays) is used to destroy cancer cells (tumour). This radiation is also destructive to the normal tissues surrounding the tumour (ICRU report 50, 1993; ICRU report 62, 1999). Therefore, it is essential that the delivery of radiation be limited precisely to the prescribed target volume.

In order to deliver quality and efficient radiation treatment service to patients with nasopharyngeal cancer, a typical radiotherapy department consisting of imaging and treatment devices is required. To allow for 3DCRT, which is considered standard radiation treatment, equipment such as computed tomography (CT) unit, treatment simulator, treatment planning computer system and treatment delivery unit, among others, are mandatory as elicited by Begnozzi et al. (2009). When a patient is diagnosed with NPC, a series of radiation treatment planning procedures will be performed. The treatment planning process starts with the acquisition of the patient's anatomical data

using various imaging modalities which include CT, MRI and Nuclear medicine imaging (Begnozzi et al., 2009). Based on the 3D anatomy information from CT due to the excellent imaging quality, which include attenuation coefficient information needed for inhomogeneous dose calculation, a patient specific radiation treatment plan is generated using a computerized treatment planning system (TPS) (Thwaites et al., 2005). In addition to CT, other imaging modalities such as positron emission tomography (PET) and single photon emission computed tomography (SPECT) can be used to provide clearer delineation of the anatomical structures. To verify the generated radiation treatment fields and patient set-up alignment, x-ray screening is performed using a simulator where the radiation beam parameters are transferred on to the immobilization cast. Prior to the start of the radiation treatment course, a quality assurance (QA) procedure is performed to verify the accuracy and reproducibility of radiation treatment set-up by portal imaging (Hurkmans et al., 2001).

2.2.1 Radiotherapy techniques

Delivery of radiation therapy puts into consideration the poorly defined boundaries of the nasopharynx which require the target volume to have broad margins for known tumour, and in addition to the nasopharynx, should include the ethmoidal and sphenoidal sinuses, the base of skull, the pterogoid fossa, the posterior two thirds of the maxillary sinuses, the pharynx walls, retropharyngeal nodes, and bilateral neck lymph nodes (Torgil, 1996). In order to cover the anatomy mentioned by Torgil (1996), two large lateral fields are conventionally used to encompass the nasopharynx and the upper portion of the nodes on the neck, while the lower nodes in the neck are treated via an anterior field (Ching, 2009; Tong et al., 1999). In cases of anterior tumour growth, Tong et al. (1999) recommends the use of an anterior face field and advocates for planning of each specific field in order to account for reduced irradiation of healthy tissue and later effects of radiation particularly in the brain. Appropriate shielding is achieved by positioning blocks at predetermined distances from bony landmarks to provide protection to vital neural organs (Chan et al., 2002). Doses are shown to be in the order of 65Gy to 70Gy given in 7 weeks, and higher doses have been reported to yield better results (Torgil, 1996; Chan et al., 2002).

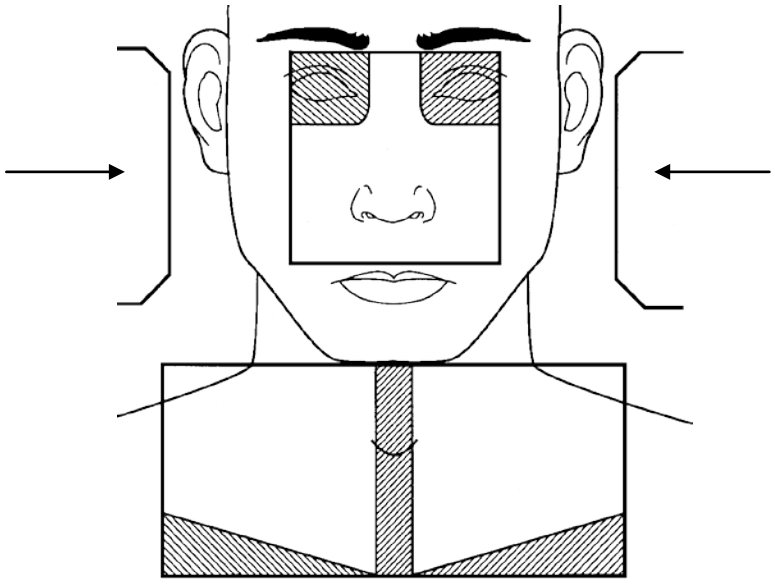

Figure 2.1: Illustration of radiation therapy technique of NPC

2.2.2 Conventional 2D radiation therapy

This is the traditional method of treatment of head and neck as developed by Ho in 1960s (Ho, 1978). It employs two parallel opposed beams for the nasopharynx and upper neck using either a cobalt 60 or low energy (6-8) MV photon beams (Spano et al., 2003; Chan et al., 2002). The whole tumour dose delivered is 60-70Gy, given in fractions of 1.8-2.5Gy for 7-8 weeks (Spano et al., 2003; Chan et al., 2002). A third anterior field is planned in case of a nasal extension or a small tumour of stage (T1-T2). This technique requires that spinal cord exclusion is done through beam modification and introduction of 6-15MeV electron beam to treat upper and posterior lymphatic cervical area (Spano et al., 2003). The bilateral lower neck and supraclavicular regions are treated by a single anterior field matched with the lateral beams, with midline shield to protect the larynx and the spinal cord. Generally, the prophylactic dose delivered is approximately 50Gy over 5 weeks and increased up to 65-70Gy in cases of confirmed nodal involvement (Spano et al., 2003).

2.2.3 Three-Dimensional conformal radiation Treatment (3DCRT)

3DCRT is considered standard method of radiotherapy delivery in the treatment of head and neck cancers to include nasopharynx (Nicolaou 1999). In this technique, the geometrical shaping of the radiation beam is planned to conform to the beams eye view of the tumour. This is made possible by the availability of functions which provides the user with accurate reproduction of anatomic features from the viewpoint of treatment source (Nicolaou, 1999). Treatment planning in the 3DCRT involves use of more fields than conventionally designed plans and these fields can have complex shapes, requiring more preparation time and can slow down the treatment process. Current linear accelerators have been advanced to accommodate the planned 3D treatment planning techniques. The advancement in the linear accelerators enable automatic radiation beam delivery set-up. This automation of set-up allows the treatment machine's movement from one field to the next enabling automatic adjustment of the rotation of its components to assume the shape and orientation of the next field. This has resulted to increased treatment efficiency in eliminating errors that could arise from mistakes by RTT. One of the major developments in the radiation treatment unit is the multi-leaf collimator which consists of a series of individually opposed motorized metal leaves within the linear accelerator. The treatment unit can be automatically programmed to assume a wide variety of shapes in seconds and allow fields to have complex shapes so that the radiation beam can be conformed to the shape of the target volume. The multi-leaves have been designed to replace the time-consuming and labour intensive customized block technique.

3DCRT has the potential to improve cancer survival rates and quality of life due to its ability to deliver higher doses to a more accurately defined tumour and at the same time lower doses to normal tissues, hence reduce treatment side effects (Thwaites et al., 2005). However, the shaping of the beams to enable conformity to the PTV is said to make 3DCRT particularly prone to set-up errors, which necessitate accurate verification of the beam shape to ensure that beam alignment and the shielding block construction and MLC position transfer to the treatment unit are correct (Begnozzi et al, 2009).

2.2.4 Intensity Modulated Radiation Therapy (IMRT)

When using conventional radiotherapy and 3DCRT, the intensity throughout the radiation field is constant. Varying the intensity across the beam and using multiple beams allow shaping of radiation beams to fit the tumour volume and delivery of complex dose distributions (Nicolaou, 1999). This technique is known as Intensity modulated radiation therapy (IMRT).

Intensity-modulated radiation therapy (IMRT) is a new radiation delivery technique that allows more precise delivery of radiation and optimization of the dose intensity to specific volumes while sparing the dose to critical normal structures (Caglar & Allen, 2007). Using IMRT in head and neck cancers is attractive because of close proximity of the tumour targets to critical normal structures such as the spine, eyes, and parotid glands. IMRT has been shown to improve local control and decrease side effects. Specifically, IMRT has shown the ability to preserve salivary function through sparing of the parotid glands (Caglar & Allen, 2007).

During IMRT treatment, a uniform dose distribution can be made to conform to the tumour by either modulating the intensity of the beam during its transit through the linear accelerator or by the use of multi-leaf collimators. This results to dose distributions that are highly conformal. The IMRT technology to allow for better dose distributions has provided the potential of improved tumour irradiation and sparing of the organs in close proximity the target volume to an extent that was not possible before; especially for concave target volume of the nasopharynx (Kristensen, 2007). IMRT is the recommended treatment of choice in cancer of the nasopharynx, where tumour dose is often limited by the surrounding critical structures such as spinal cord (Lee et al., 2002). IMRT has provided a solution for its ability to provide tight dose gradients around the target volume enabling higher doses to be delivered to the tumour while reducing the dose to surrounding critical organs and radiosensitive tissues such as salivary glands, ears and optic chiasm (Kristensen, 2007).

IMRT offers the potential for improving local control and sparing non-involved tissues. Lee et al. (2002), reported a locoregional recurrence free survival of 97% at a median follow-up of 31 months in a study group involving 67 patients with nasopharyngeal carcinoma treated with IMRT. In this study group, acute side effects were found to be well tolerated with 76% of patients having G1-2 toxicities. The results of a follow up at 24 months indicated that 92% of the patients had Grade 0-1 xerostomia. Lee et al. (2002) indicate that nearly all patients were able to complete the planned chemotherapy implying that IMRT optimize the delivery of concurrent chemotherapy in patients with nasopharyngeal carcinoma. Despite these promising results, Lee et al. (2002) caution of the use of IMRT for it is still a new technology whose clinical data are still in the preliminary stage; employing complex technology; and labour-intensive and thus prone to potential errors. Quality assurance of IMRT is said not to be standardized (Lee et al., 2002).

2.2.5 Radiation Treatment outcome of NPC

The standard treatment for NPC is radiotherapy alone for early stage disease (stage I & II) and combined chemo-radiation therapy for advanced disease (stage III & IV) (Lee et al., 2002) such as in the study group. Advanced stage NPC has been reported to have favourable response to aggressive radiotherapy strategy with the outcomes with radical radiotherapy alone in terms of loco-regional control, disease free survival, and overall survival varying due to varied radiotherapy techniques. Yi et al. (2006) indicate that external beam radiotherapy has been the first choice in treating NPC at the Academy of Medical Sciences in Beijing, China with a resultant 10 year disease specific survival, relapse-free survival, and distant metastasis-free survival of 98%, 94% and 98% for early stage patients. The Yi et al. (2006) study gave a boost irradiation to the residual disease after 70-72Gy of EBRT to more than 80Gy and were able to achieve a local control of 80.8% in patients who had residual primary lesions, similar to that obtained with primary lesions that completely disappeared at 70-72Gy. Similar conclusions in favour of a boost dose for a positive residual NPC lesion is shared by Yan, Qin and Hu et al. (1988 & 1989). However, Yi et al. (2006) indicate that even for early stage NPC, a proportion of patients present with radio-resistant tumours and need more than 70Gy for local control,

which imply that high doses would be beneficial for this group of patients. Al-Saraff, LeBlanc and Giri (1998) reported a 30-45% 5 year survival rate in patients with stage III and stage IV NPC with radiotherapy alone. A more recent retrospective study by Xu, Pan and Wu et al. (2010) involving 1706 patients with NPC, who underwent treatment at Fujian cancer centre in China during the period 1995 to 1998, gives an overall 5 year survival rate for stage I, II, III & stage IV as 100%, 75.9%, 66.5% and 49.3% respectively. Combined chemo-radiation therapy is reported to have improved a 5 year survival benefit with survival of patients treated with or without neoadjuvant chemotherapy being 68.9% and 63.7% respectively. More favourable results on concurrent chemo-radiation therapy studies were reported by Chan et al. (1998) in an intergroup study for stage III and IV NPC involving 138 patients randomised to receive radiotherapy alone or with concurrent cisplatin and adjuvant cisplatin and 5-FU. The radiotherapy technique was 2Gy/fraction to 70Gy in 7 weeks. In the concurrent arm, cisplatin 100mg/m^2 was given every 3 weeks for 3 doses during radiotherapy and cisplatin 80mg/m^2 on day 1 and 5FU 1gm/m^2 was given on day 1-4 given for 3 cycles after concurrent chemo-radiation therapy was completed. The median progression free survival was 13 months in the radiotherapy arm compared to 52 months in the concurrent chemo-radiation arm. The 2 year survival was 55% in the radiotherapy arm compared to 80% in the chemo-radiation therapy arm. This implies that the use of concurrent chemo-radiation therapy using cisplatin followed by adjuvant cisplatin and 5-FU is favourable for these patients presenting with NPC stage III & IV as in the study group (Chan et al., 1998).

2.3 Need for Portal imaging in clinical practice

The results of radiotherapy are determined by many factors such as biology of the tumour, stage of the disease, dose parameters, and also by the geometry of the radiation beam (Milecki et al., 2001). In the head and neck region, the requirement for accuracy and reproducibility of treatment set up is important as it is one of the major criterion of quality assurance in radiation therapy. It has been found that reduction of an absorbed dose in a significant portion of the gross tumour volume (GTV) may decrease the probability of local control of tumour (TCP) while on the other hand, additional radiation

to healthy tissues arising from geometric errors may increase radiation toxicity (Milecki et al, 2001). Thus, the verification of field alignment by portal imaging can increase the accuracy and reproducibility by identifying radiation beam alignment errors.

It was demonstrated early in 1976 that increasing the frequency of portal verification or check films during the course of therapy can increase the accuracy and reproducibility by identifying radiation beam geometric errors thus improved clinical outcome (Marks et al., 1976). Current megavoltage radiation treatment units have the capacity for electronic portal imaging devices (EPIDs) which enable the viewing of a digital image of the field under treatment and allow for the quick correction of any misalignment before treatment is commenced. However, treatment centres with radiation treatment equipment without EPID capability use conventional portal or check films as a routinely available technique (Lirette et al., 1995).

Patient specific quality control is essential in the delivery of radiation treatment to patients with nasopharyngeal carcinoma. Assessment of check films during radiation treatment in patients with cancer of the head and neck region is an important quality assurance process (Fogarty et al., 2001). Its goal is to detect and correct any significant errors in field placement thus prevent geometric miss of the target volume during radiation treatment (Suter et al., 2000). Analysis of check films in many departments rely on visual comparison of a check film with a reference image (Hurkmans et al., 2001). This comparison is done on weekly basis throughout radiation treatment once satisfaction with patient set up is established in the first week (Suter et al., 2000).

Generally the position of the centre of the radiation beam(s) relative to the patient's anatomy, obtained from the simulator or digital reconstructed radiographs (DRRs,) is verified using the actual treatment fields thus the portal image provides information about the correct beam aperture or positioning of the blocks (Suter et al, 2000). Portal films are thus an important component in the overall QA in the radiation treatment to patients with head and neck cancer (Fogarty et al., 2001).

In general, several aspects that need to be incorporated in radiation therapy verification as highlighted by Van Elmpt, McDermott, Nijsten et al. (2008) include, procedural verification using well documented protocols and workflow, set-up verification measurements of the patient position and also verification of the dose delivered to the patient. This study concerns set-up verification of radiation therapy and thus dose verification is beyond the scope of this study.

Knowledge of the random and systematic errors of patient set-up for a specific treatment technique is important for it can be used for the adjustment of radiation treatment margins for patients with head and neck cancer (Herman et al., 2000; Royal College of Radiologists, 2008; Hurkmans et al., 2001).

2.3.1 Portal verification in conventional 2D radiation therapy

In conventional RT, treatment verification is by means of the treatment beam from either a cobalt 60 or the older version linear accelerator. Treatment beams are used to obtain images to verify the accuracy of set-up in the first radiation treatment session after the patient is positioned on treatment couch as initially planned (Thwaites et al., 2005). In subsequent sessions, the patient is positioned with the aid of lasers and beam alignment marks on the cast. Routinely, films are taken once a week to verify the reproducibility of the set-up (Hurkmans et al., 2001). Although portal verification using film provide useful information, the film method provide information that can be examined after treatment, and if necessary, a correction is made at the following treatment session, this is viewed as a disadvantage when compared to EPID technology which provide online information (Herman et al., 2000).

Langmack (2001) indicates that X-ray film has conventionally been used as a medium for portal imaging with the exposure conditions depending on the distance between the radiation source and the film, the thickness of the patient and the field size. This necessitates the production of port film acquisition technique charts that give the required exposure as a function of these parameters (Lee & Glasgow, 1998).

Historically, radiation therapy portal films were industrial direct exposure films (Haus, 1998) but the introduction of metal screens into the radiographic cassette meant that the diagnostic x-ray films could be used in these cassettes (Hammoudah & Henschke, 1977; Droege & Bjarngard, 1979a; Droege & Bjarngard, 1979b). The composition of the metal screens has been shown to improve the image quality (Droege & Bjarngard, 1979b) as has the films used in these cassettes (Roberts, 1996), and Kutcher et al. (1994) suggested at the time that portal imaging using film was considered the standard for radiation treatment localisation. Although these portal film systems provide high quality images, there is evidence that simple visual inspection of these images is unable to reliably identify radiation field placement errors of up to 5mm (Perera et al., 1999). It is therefore argued, in favour of digital imaging, that computerised tools for measuring set-up errors are required (Perera et al, 1999) in high precision radiation therapy.

2.3.2 Portal verification in recent 3DCRT and IMRT

In order to confirm that the delivery of 3DCRT and IMRT is as planned, correct verification of radiation beam in the actual setting (both during the first and daily treatments) is required. Begnozzi et al. (2009) indicate that this is achievable by making a comparison between the simulator or DRRs images and actual images obtained with the treatment unit and confirm the correct patient positioning, volume and treatment geometry. EPID technology as explained in section 2.1.3. can be used in evaluation of treatment set up relating to field aperture and anatomy in a portal image to that in a reference image, and choosing a course of action to reduce any errors present (Herman et al., 2000). EPID capability to provide online correction means that a pre-treatment image is captured, reviewed and corrections applied before treatment continues (Herman et al., 2000). The same author, (Herman et al., 2000), however cautions that the use of a new technology, even to accomplish a simple goal, cannot be taken lightly and that there should be specific implementation goals, clinical procedures, and protocols before it can be successfully brought into the clinic. The EPID is subjected to stringent system specific calibration procedures to ensure that the beam alignment is within 2mm at a number of gantry angles and detector positions as part of daily QA program (Herman et al., 2000; Meertens et al., 1990; Visser et al., 1990) indicate that system specific calibration

procedures should be provided by the manufacturer or supplier. Herman et al. (2000) indicate that the Las Vegas phantom has been used in acceptance testing and in the continuing quality assurance of EPID. The authors indicate that visualising of certain holes of the aluminium block with holes of various depths and diameters is commonly used to check specific resolution for a given linear accelerator treatment beam. The EPID is thus a powerful QA tool that enables the treatment team to perform patient beam alignment verification, organ and target motion studies, compensator design, treatment unit and patient dosimetry checks within a short timespan (Herman et al, 2000).

2.3.3 Electronic portal imaging

It is widely documented (Hurkmans et al., 2001; Mileusnic, 2005; RCR, 2008) that in the recent years, electronic portal imaging devices (EPIDs) have become popular in clinical use in the detection and management of geometric errors during radiation therapy. Its attachment to the treatment unit makes it more suitable and readily available for real time verification during radiation treatment (Hurkmans et al., 2000). A study by Hunt, Schiltheiss, Desobry et al. (1995) suggest that due to the small amount of time needed to image with EPID, EPID is a more accurate reflection of patient set-up than film. The authors further indicate that EPID is of use in cases that require rapid set-up such as emergency radiation treatment for pain or paediatric patients for its capability to provide immediate feedback, hence considered an excellent alternative to film (Hunt et al., 1995).

Although initially EPID technology was reluctantly accepted in the market because of poor image quality, recent advances in flat panel display EPID have been associated with faster image acquisition and superior image quality (Mileusnic, 2005). Another powerful feature with the flat panel display, as pointed out by several authors, (Mileusnic, 2005; Van Elmpt et al., 2008; Herman et al., 2000) is that the images are in digital format which allows the application of software tools. These tools allow for processing (to extract information relevant to verification and the managing) by picture archival and communication system (PACS) specially designed for radiation treatment (Van Elmpt et al., 2008). The EPID has been developed to enable computerised comparison of images for detection of field placement errors in recent 3DCRT and IMRT units and currently its

use in dose verification is being realised (Mileusnic, 2005; Royal College of Radiologists, 2008). The use of EPID for dose verification has evolved from the theory derived by Boyer, Antonuk, Fenster et al. (1992) on the theoretical characteristics of portal imaging performance, where the exit radiation beam contains more information than is extracted by conventional portal imaging systems.

2.3.4 Image guided radiation therapy (IGRT)

Image guided radiation therapy is a concept utilising imaging to define and delineate the target volume in 3D and to evaluate the treatment response (Jaffray & Dawson, 2007). Frequent imaging in the treatment room during a course of radiation therapy, with decisions made on the basis of imaging, is regarded as IGRT (Jaffray & Dawson, 2007). IGRT allows changes in target position, size, and shape to be measured during the course of therapy, with adjustments made to maximise the geometric accuracy of radiation delivery, reducing the volume of healthy tissue irradiated, thus permitting dose escalation to the target volume (Jaffray & Dawson, 2007; Herman et al., 2001).

In order to achieve IGRT, a source of imaging is required, which could include computed tomography (CT), kilovoltage (kV) x-ray and megavoltage (MV) or ultrasound (Herman et al., 2000; Royal College of Radiologists, 2008). These imaging modalities are utilised in IGRT as a routine procedure used for positioning at each treatment session (Herman et al., 2000) and utilises the availability of software technology, also present in EPID, for automatic matching of reference images and portal images (Herman et al., 2000; Royal College of Radiologists, 2008; Hurkmans et al., 2001).

These geometric advantages increase the chance of tumour control, reduce the risk of toxicity after radiotherapy, and facilitate the development of shorter radiotherapy schedules (Jaffray & Dawson, 2007; Herman et al., 2000). By reducing the variability in delivered dose across a population of patients, IGRT should thus translate to improved interpretation of clinical trials in future (Jaffray & Dawson, 2007).

2.4 Equipment and Patient QA

2.4.1 Recommended QA for cobalt-60 unit

The World Health Organisation (1988) stated that it was necessary for all radiation therapy providers to implement quality assurance. Quality assurance (QA) in radiation therapy is defined as 'all procedures that ensure consistency of the medical prescription, and the safe fulfilment of that prescription, as regards the dose to the target volume, together with minimal dose to normal tissue, minimal exposure of personnel and adequate patient monitoring aimed at determining the end result of the treatment' (Thwaites et al in Podgorsak, 2005:407; WHO, 1988). According to Fogarty et al. (2001), an effective quality assurance strategy for radiation therapy must assure that imposed criteria are met and if not, then corrective action must be quickly taken based on knowledge about the errors (uncertainties) and their consequences.

The errors that arise in the process of radiation therapy are difficult to identify retrospectively because the effects usually appear a long time after the radiation treatment delivery and because the symptoms can be diffuse and be similar to problems common also after delivery of correct radiation treatments (Peiffert, Simon & Eschwege, 2007). The investigation of treatment errors can facilitate the formulation, introduction and/or adoption of QA procedures to overcome their occurrence (Thwaites et al., 1995). It helps the staff involved to update their knowledge in QA procedures and develop new ideas/methods in QA and thus improves the work practices of the department (Peiffert et al., 2007).

Comprehensive guidelines have been developed by American Association of Physicists in Medicine in the AAPM Task Group 40 (1994); AAPM Task Group 53 (1998), Medical Physicists such as the Thwaites-led groups (Thwaites et al., 1995 & 2005) which form the basis of reference when developing local QA guidelines. In general, QA of the radiation therapy treatment includes treatment unit QA and patient specific QA.

Routine QA on cobalt-60 is essential to monitor the stability of its performance so that any errors can be detected as early as possible. Cobalt-60 QA involves several mechanical tests, safety interlocks, and dosimetry consistency checks (IAEA, 2008: CAPCA, 2007; AAPM Task Group 40, 1994; Thwaites et al. 1995 & 2005). Mechanical tests involve inspecting the accuracy of various physical components of the cobalt-60 such as cross-hair alignment and the coincidence of the light and radiation fields, and laser alignment need to be within 2mm (Thwaites et al. 2005; IAEA, 2008). These tolerance levels, however, can be made more stringent in order to improve clinical practice (CAPCA, 2007). Dunscombe, Johnson, Arsenault et al. (2007) have formulated QA guidelines for cobalt-60 that recommend a tolerance level for physical components like crosswires, lasers and field size indicator among others to be within 1mm. Other checks include safety interlocks which involve checking the functionality of various safety control systems such as door interlock and emergency switch; dosimetry consistency involves calibrating various dosimetric parameters such as radiation output and properties of beam modifiers (Dunscombe et al., 2007; Thwaites et al., 2005). In practice, cobalt-60 QA is performed daily, weekly, monthly and annually, with different levels of QA procedures (Dunscombe et al., 2007; Thwaites et al., 2005). A detailed sample QA of cobalt-60 by the AAPM TG 40 with recommended test procedures, test frequencies and action levels is given in 'Appendix I' which when adhered to, ensures that the equipment performance will provide the levels of accuracy required in the delivery of radiation treatment to patients. Equinox cobalt-60 QA practices were found to be in place at the study site as indicated by the content of QC document 'Appendix II' and the unit was still under warranty with once a year maintenance contract by the manufacturer for a period of 5 years.

2.4.2 Simulator QA

Thwaites et al. (2005) notes that treatment simulators replicate the movements of isocentric cobalt-60 and linear accelerator units and are fitted with identical beam and distance indicators. Hence all measurements that concerns cobalt-60 and linac units also apply to the simulator and should be quality controlled in a similar manner for if the mechanical/geometrical parameters are out of tolerance on the simulator, this will affect

treatments of all patients whichever treatment unit they are subsequently treated on (Thwaites et al, 2005). Simulator QA was found to be in place at the study site as indicated by the content of QC document 'Appendix III' and was still under warranty with twice a year maintenance contract by the manufacturer for a period of 5 years.

2.4.3 Patient specific QA

Patient specific QA practices are performed prior to start of a radiation treatment course to verify the delivery accuracy of the plan (Thwaites et al 2005). Portal imaging forms one of the QA procedures for the verification of patient specific radiation treatment on cobalt-60 (Thwaites et al 2005) and has been used to quantify radiation beam delivery in head and neck patients. The analysis of the measurement and the calculation can be performed using QA softwares or an in-house derived method, and the measurements should be in agreement with the set criteria that satisfy the clinical departmental protocol, national standards or international guidelines (Thwaites et al 2005).

2.4.4 Portal imaging QC in NPC

A radiation treatment consists of one planning session and multiple irradiation sessions (Stroom & Heijmen, 2002). In the planning phase, the patient geometry is visualized using CT or simulator images. The visualized structures are the basis for construction of the treatment plan and the intention is to deliver this plan in all the radiation treatment sessions to a target volume (Stroom & Heijmen, 2002) with high accuracy and reproducibility. Van Elmpt et al. (2008) indicates that observing quality control (QC) procedures before and during radiation treatment has the potential to ensure a high level of accuracy and reproducibility necessary for treatments designed to achieve adequate tumour control and reduction of normal tissue complications. Milecki et al. (2001) concurs that a QC of the geometric accuracy of treated portals during radiation treatment results in higher quality of treatment and thus lead to increased therapeutic gain.

'Quality control' is defined as the regulatory process through which the actual quality performance is measured, compared with existing standards, and the actions necessary to

keep or regain conformance with the standards (Thwaites et al. 2005). In radiotherapy, Thwaites et al. (2005) suggests that the best way to implement the requirements proposed for radiation providers by radiation legislation or institutional protocol is to use a quality system covering the entire radiotherapy process, describing a quality system as a system of organisational structures, procedures, processes and resources required in QC and described in a quality manual. Portal verification QC can therefore be achieved by developing and making use of a quality system for the verification of radiation therapy to the head and neck region (Thwaites et al. 2005). Because there is no single technology or strategy currently in existence for the verification of radiation treatment, each radiation treatment department need to adopt the most suitable for their local situation according to the available technology.

Fogarty et al. (2001) indicate that a portal imaging protocol is in place at their department which ensures that portal images are done weekly for radical head and neck patients. In addition Fogarty et al (2001) further mentions that these portal films are examined during the weekly portal film review in which a consultant, preferably the prescribing or the registrar, would exhibit the latest portal verification film alongside the relevant simulation film on an x-ray light box in view of all attendees. This weekly procedure provided a forum for peer review where all radiation oncologists assessed the simulation plans of others, which in some cases , led to changes of field size and technique as well as acting as an educational forum (Fogarty et al., 2001). From this weekly portal film peer review, a QC document which Fogarty et al. (2001) refers to as a ‘chart round check list’ was introduced which allowed for a quick check of the entire radiotherapy process. Some of the checks read patient history dictated and typed; letter to referring doctor sent out; pathology report filed; port film checked; planning of new technique on track;…and follow up appointments scheduled, and in some areas of shortcomings, corrections were done as appropriate (Fogarty et al., 2001). From this information, it can be deduced that the weekly portal film review eventually translated to a complete QA in the radiation oncology unit and the author recommends adoption of such a model by other departments that do not yet have a system in place (Fogarty et al., 2001). A similar practice is reported by Suter et al. (2000) to be in practice at the Royal Marsden Hospital in the UK. The

authors report that weekly multidisciplinary meetings are held to review all simulator and treatment unit portal films by the consultant, senior and junior registrars.

2.5 Sources of radiation beam alignment errors

Hurkmans et al. (2001) note that a number of sources of random and systematic errors can be distinguished. These are identified to be mainly due to equipment mechanical shortcomings (e.g. laser misalignment); patient related (e.g. skin mark movement), or fixation related (e.g. patient mobility) (Hurkmans et al., 2001). One other major factor identified influencing the set up uncertainty, is the accuracy with which the radiation therapy technologists are able to position the patient using the set up marks or documentation. Set-up ability is said by Hurkmans et al. (2001) to be influenced by the experience, previous training and concentration of the RTTs, and the time available to position the patient. The physical and mental state of the patient also needs to be considered for it also influences the set up accuracy (Hurkmans et al., 2001).

As in most patient set-up studies, the geometric inaccuracies are referred in this study as errors (Mileusnic, 2005). Several studies (Hurkmans et al., 2001; Vos, Van Riel & De Winter, 1997; Huizenga et al., 1988) among others have documented systematic and random errors in the head and neck region indicating systematic to be associated with transfer error from planning to treatment unit while random being due to difference in day to day treatment set up. Appropriate pre-treatment QA can render these errors small and the understanding of the magnitude of these errors can thus be used to guide in margins used or adjustments required in treatment planning to cover for these set up inaccuracies. Therefore, the reduction of set-up errors by means of set-up correction protocols is required in clinical practice (Hurkmans et al., 2001).

2.5.1 Studies on radiation beam alignment errors

In EBRT, set-up errors are measured using portal imaging by applying megavoltage film or an electronic portal imaging device (EPID) (Hurkmans et al., 2001). Although portal imaging guidelines indicate acceptable beam alignment to be within 4mm, it is possible to achieve positioning accuracy of approximately 2mm in head and neck region because of the compact nature of the head and neck region and the use of good immobilisation (Royal College of Radiologists, 2008; Thwaites et al., 2005). In the head and neck region, the standard deviation of the systematic and random deviation for current applied treatment techniques is reported to ranges from 1.6mm-4.6mm and 1.1mm-2.5mm (Hurkmans et al., 2001). Some of the studies done using portal film method and EPID method include Huizenga, Levendag, De Porre et al. (1988); Mitine, Dutreix & Van der Schueren (1993); Weltens, Kesteloot, Vandevelde et al. (1995); Willner, Hadinger, Neumann et al. (1997); Bel, Keus, Vijlbrief et al. (1995); Gildersleve, Dearnaley, Evans et al. (1995); Vos, Van Riel & De Winter (1997); and Yan, Wong, Vicini et al (1997).

2.5.2 Port film studies

Huizenga et al. (1988) in their study involving 22 patients found deviations measuring 2.1mm systematic and 2.1mm random; Mitine et al. (1993), 27 patients, deviations of 4.4mm systematic and 2.3mm random; Welten et al. (1995) involved 29 patients and measured deviations of 2mm systematic and 2mm random and Willner et al. (1997) in their study involving 43 patients measured deviations of 3.5mm systematic and 2.1mm random. It is however pointed out that the accuracy of matching EPID images with matching software or megavoltage film with visual inspection has some intra and inter-observer variations which necessitate careful attention to measurement method used in order to reduce the magnitude of observer variability (Bissette et al., 1995; Boyer et al., 1992).

2.5.3 EPID studies

In their studies using EPID verification systems, Bel et al. (1995) studied 21 patients and found systematic deviations of 1.7mm and random deviations of 1.6mm; Gildersleve et al. (1995) in their study involving 26 patients documented systematic deviations of 2.2mm and 1.5mm random; Vos et al. (1997) in a study involving 12 patients found systematic deviations of 1.6mm and random deviations of 1.5mm; and Yan et al. (1997) involved 12 patients and found deviations of 1.9mm random and 1.4mm systematic.

2.5.4 Studies on consequences of radiation beam misalignment

Portal film and EPID studies are in concurrence with earlier studies that the consequences of radiation beam alignment errors can be serious. Goitein and Busse (1975), using dose volume histograms and a radiobiological model, found that patient positioning relative to the radiation beam should be within 2mm to ensure a normal tissue complication probability (NTCP) of 1%. Similarly, Brahme (1984), using radiobiological model, found that the tumour control probability would decrease between 3-7% for a 2mm misalignment in radiation beam. These studies (Goitein & Busse, 1975; Brahme, 2005; Brahmel, 1984) suggest that the beam alignment should be localized with respect to the patient anatomy to within 2mm. The quantified accepted value of 2mm is considered standard in current practice of treatment to the nasopharynyx and other head and neck cancer with the use of adequate immobilization as recommended by several authors of recent literature on the subject (IAEA, 2008; RCR, 2008; CAPCA, 2007; Thwaites et al., 2005; Hurkmans et al., 2001).

2.6 Conclusion

The current chapter has reviewed literature relevant to this study. The next chapter explains the research methodology designed by the researcher. It describes procedures followed in order to generate numeric data that would answer the study concerns while limiting research bias

Chapter Three

Research design and methodology

3.1 Introduction

Chapter two provided a theoretical framework to support the study and an interpretation of the current and relevant literature accessible to the researcher. This chapter (chapter 3) explains the research design formulated in order to carry out data collection which would enable analysis as planned for this study. A pilot study was used to provide information that allowed for the method used in the collection of data. The ethical considerations are discussed, validity and reliability are also addressed.

According to Leedy and Ormrod (2005), the purpose of research is to learn what has never been known before; to ask a significant question of which no conclusive answer has previously been found; and through the medium of collecting relevant data and their appropriate interpretation, to find an answer to that question. This study therefore was conducted to answer a research question resulting from a research problem.

3.2 Research problem

Quality control of radiation treatment is a standard practice in the delivery of accurate and reproducible radiation treatment. In the absence of QC procedures, the accuracy and reproducibility of radiation treatment cannot be quantified. Portal imaging is one of QC procedures for the verification of radiation treatment with the primary role of detecting radiation treatment beam delivery errors. This is achieved by comparing images from the delivered radiation treatment against the images of the planned treatment (Royal College of Radiologists, 2008).

The study site does not have a QC process for verification of radiation treatment. Radiation treatment verification portal films are therefore not routinely done and there has never been such a study on accuracy and reproducibility of treatment setup conducted. Lack of a QC protocol on radiation treatment verification in patients with

head and neck cancer was thus the problem in this study which led to the research question.

3.2.1 Research question

According to Maree (2007), a research question specifies what intrigues one, and focuses on what one will study. It further becomes a beacon that guides a researcher during the period of research. The overall research question that is addressed by this study is:

'What is the accuracy and reproducibility of treatment to patients with nasopharyngeal cancer on the Equinox Cobalt-60 unit?'

Three further sub-questions addressed are:

1. How accurate is the treatment field placement on Equinox cobalt-60 radiation therapy unit?
2. How reproducible is the treatment set-up during the period of radiation therapy using the cobalt-60 unit?
3. What are the recommended QC processes that ensure radiation therapy is accurate and reproducible on a cobalt unit?

3.2.2 Research design

To answer the research question in this study, measurements and analysis of the simulator and cobalt 60 unit check films were required. A quantitative methodology approach was found suitable because it employs measurements and the generation of data using standardized predetermined criteria (Leedy & Ormrod, 2005; Bogdan & Biklen, 1998). These data were collected within a controlled environment using identified standard equipment used in radiation therapy planning and treatment (see section 3.7.3; 3.7.4). The mathematical process is the norm for analysing these data, and the final results are expressed in statistical terminologies (Hicks, 2004; Golafshani, 2003; Charles, 1995). The use of measurements that generate numeric data was chosen to ensure that the

evidence obtained answered the research question as unambiguously as possible (Burns & Grove, 2003).

A summary of the relationships between steps of research process is mapped in the circulatory, flow diagram developed from that of Leedy and Ormrod (2005). The research question is the core of each step.

Figure 3.1*:* A schematic diagram showing the research process
(Developed from Leedy & Ormrod (2005)

3.2.3 Pilot Study

A pilot study was conducted to check the method and proposed procedures of the data collection process and develop a suitable simulator and treatment unit check film protocol for the study (Appendix III & IV). This protocol included: standardisation of the patient positioning and set-up, exposure factors and imaging (simulation and treatment unit check films) techniques.

Van Teijlingen and Hundley (2001) give some of the advantages of conducting a pilot study to be: advance warning about where the main research project could fail; where research protocols may not be followed; developing and testing research instruments; designing a research protocol; assessing whether the research protocol is realistic and workable; whether proposed methods or instruments are inappropriate or too complicated and determining what resources (finance, staff) are needed for a planned study; as well as, training a researcher in as many elements of the research process as possible.

A pilot study is indicated to be carried out on fewer members of the relevant population, but not on those who form part of the final sample (Hulley, 2007). For purposes of this research, this pilot study was conducted on three patients in April 2011 before commencement of the main study in May 2011 in order to design set-up (see Figure 3.2 below) for the acquisition of simulator and cobalt 60 treatment unit images that would result in the same image magnification, stipulate the exposure factors to be used during acquisition of simulator and cobalt-60 treatment unit check films, test the data capture format upon which to record measurements and data entry , as well as train research assistants on particular roles to be engaged in during the data collection period.

The pilot study found an initially developed data capture tool during proposal development to be inadequate. This is due to the amount of data which needed to be captured that included participants' demographic information and tumour characteristics in addition to the measurements done on the simulator and the Equinox cobalt-60 treatment unit check films. The inadequacy of the data capture tool necessitated direct entry of data onto an excel worksheet.

Figure 3.2 demonstrates the set-up configuration developed during the pilot phase that enabled symmetry of the simulator and treatment unit films in order to achieve images with same magnification.

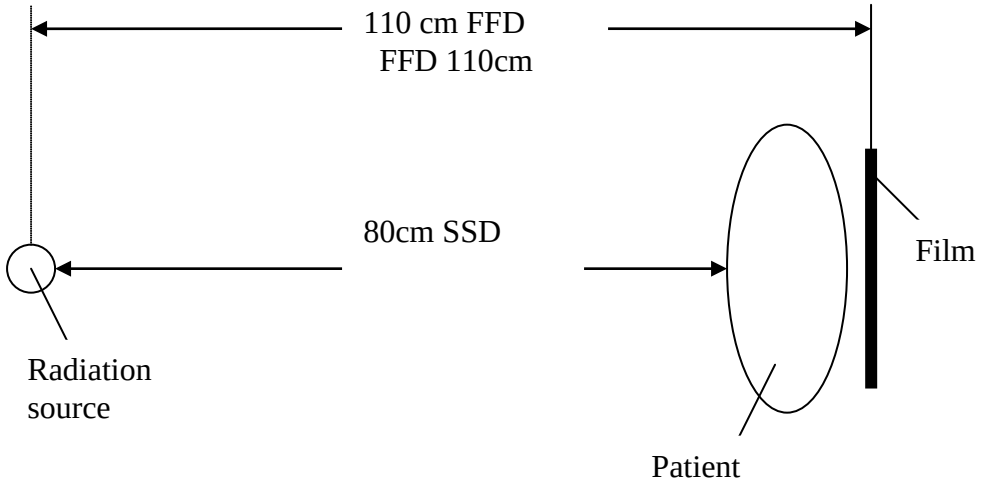

Figure 3.2: Schematic representation of simulator and cobalt-60 check film acquisition

3.3 The study site

The study site is the radiation therapy department at the largest national referral and teaching hospital in Kenya. It is the only state run department with the capacity to provide radiation therapy services to patients with cancer. The department was started in 1968 and currently has two cobalt-60 isocentric treatment units. The two cobalt-60 units serve the entire country with a population of over forty million people.

3.4 Study population of patients with nasopharyngeal cancer

It was indicated in chapter one that like many other developing countries, the study site does not have a national cancer registry which explains the unavailability of population based statistics for this study group. The researcher therefore worked with information from the study site departmental records, which indicated that the number of patients treated for cancer of the nasopharynx was 150 in 2008. Based on this number, the number of patients with cancer of the nasopharynx and any other head and neck cancer treated using the same external beam technique would be approximately twelve patients per

month. Thus, it was expected that the population between the period May 2011 and March 2012 would be 132 patients.

3.4.1 Sample selection

In preparation for this study, the researcher had to go through the departmental record booking list of patients waiting to start radiation treatment to the head and neck region. A three months booking indicated that the number of patients falling within the enrolment criteria was lower than expected (see section 3.4). The researcher thus opted to conduct the study using a purposive sample which requires the researcher to select research participants that present and are able to participate in the phenomena to be investigated (Leedy & Ormrod, 2010; Brink et al., 2006).

The researcher, based on the available subjects, decided to take the entire group as the study sample having considered the inclusion and exclusion criteria in order to include as many participants as available. Sequential enrolment was thus done starting May 2011 up to March 2012. To provide the broadest range of information possible, all patients receiving radiation therapy to the head and neck region who met the inclusion criteria (see section 3.4.2) were included in the study. In this way, the results from this study group can be more confidently assumed to be applicable to the wider population (Hicks, 2004). During the period of data collection thirty five patients were realised as the study sample. Naiyanet et al., (2007); Pehlivan et al., (2009); and McJury et al. (2006) did related studies involving nine, twenty and twenty five participants respectively.

3.4.2 Inclusion criteria

Inclusion criteria were defined by the researcher to enable for sequential enrolment of all adult male and female patients over 18 years of age; with confirmed diagnosis of nasopharyngeal carcinoma and other head and neck cancer treated with the same technique in the same area; prescribed to be immobilised using a mask; assessed at the radiotherapy clinic and scheduled to receive curative radiation treatment to the head and

neck region; scheduled for radiotherapy within the approved study period; and who gave written informed consent to participate in the study.

3.4.3 Exclusion Criteria

There were some exclusion criteria for patients receiving radiation therapy to the head and neck area though treated using same beam arrangement. These were patients scheduled for radiotherapy under a palliative regime; under the age of 18years; those with inability to make own decisions; those immobilized using different immobilization system (for example forehead and chin strapping); and those not giving consent to participate in the study.

3.5 The study

A prospective study was performed on thirty-five (35) patients with nasopharyngeal and other head and neck cancer meeting the enrolment criteria. These patients were all treated on Equinox cobalt-60 radiation therapy unit during the period 2nd May 2011 and 24th March 2012. This was within the approved period for data collection by the Research Ethics Committee of the training institution (Appendix X) and that of the Ethics and Research Committee of the study site (Appendix V). The study group comprised of patients with cancer of the nasopharynx or any other head and neck cancer treated using the same radiation beam arrangements. All received radiotherapy treatment with curative intent using right lateral, left lateral parallel opposed radiation beam portal and anterior lower neck radiation beam portal.

3.6 Data collection process

Data from 35 participants enrolled were collected using the study protocol (see Appendix III & IV) developed following the results of a pilot study. The Appendices acted as a guiding tool which was necessary to develop in order to enable the researcher to collect relevant information. SASSA (2008) defines data collection tools as strategies used to collect information. The study protocol in this study was used as a tool which provided a methodological way of obtaining simulator films and treatment unit port films. For all

patients in the study, one right lateral simulator film was taken prior to treatment as part of the planning process and is used as verification of intended treatment field. The 35 simulator films were coded as 'data set A'. The simulator films were used as the reference standard against which the Equinox cobalt-60 treatment unit check films would be compared. During the course of their radiotherapy treatment, a treatment unit check film was taken once a week for the first four weeks indicated as 'plan 1' or 'large volume'. These treatment unit check films were coded as 'data set B'.

This data collection method was guided by the research design (quantitative) which involves measurement and analysis using statistical methods in order to answer the research question. In this paradigm, the research question, data collection and methods used, and its presentation, are all considered in the study designing stage (Leedy & Ormond, 2005). This relationship can be depicted in the following illustration which allows one to go back and forth between the stages of the research process:

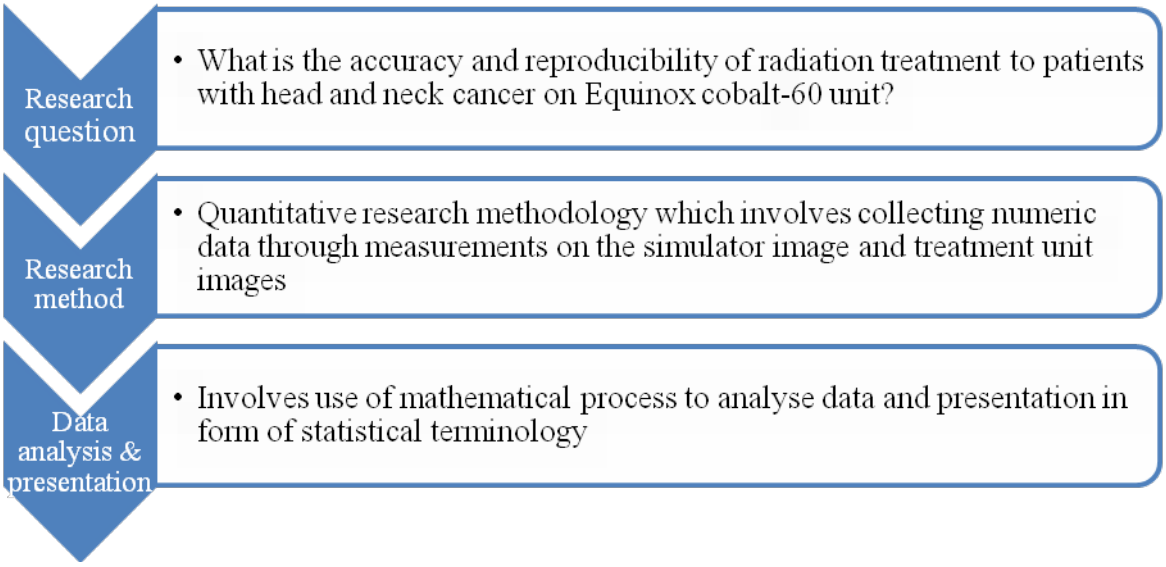

Figure 3.3: Illustration of relationship of different steps that inform research design

3.7 Method/Procedure

It is documented by Mouton (2001) that there is need to present the data collection process as accurately and in as much detail as possible, as a historical record for the researcher and other possible researchers. This requirement is thought to be met in this study in following the method and procedure stated. The following procedures were followed to collect, record, process and analyse the data.

3.7.1 Immobilisation

All patients in this study group were immobilised using thermoplastic orfit material before simulation and radiation treatment on Equinox cobolt-60 radiation treatment unit. There were two different head and neck base plates and Orfit materials available and used in this study. One type of the Orfit is a factory pre cut 3 point immobilisation material (Orfit 'A') the second is a rectangular flat sheet of Orfit material (Orfit 'B') which is trimmed to shape (using a template for uniformity) in order to allow for fixation onto the head and neck base-plate. Both types of base plates and Orfit materials were used for this study group.

Immobilisation devices are made to keep the patient in the same position during radiation treatment to ensure accurate reproducibility in the radiation treatment set-up and are said to be a reliable means of reproducing the patient position from simulation to treatment, and for the subsequent radiation treatments (Rovirosa et al., 1995; Barrett et al., 2009; Dobbs, Barrett & Ash, 1999; Cottrill & Nutting, 2003).

3.7.2 Simulation

Simulation of patients in radiotherapy is done to ensure that the radiation beams used for treatment are correctly chosen and properly aimed at the intended area (Dobbs et al., 1999:69). To achieve this in the study group, custom made immobilization cast was made for each patient to ensure that the radiation beam geometry and acquisition of treatment data are accurate and consistent (IAEA, 2008). A conventional simulator is available at the study site and thus was used for simulation of radiation treatment fields. The simulator used is an Ocentra simulator capable of providing fluoroscopic images as well as radiographic hard copy images. Conventional simulation units are based on radiotherapy treatment unit geometry, thus the simulation procedure on the study group was used as an indication of what would be achievable at the radiation therapy treatment unit (Baker, 2006; IAEA, 2008).

3.7.3 Acquisition of Simulation films

Simulator images were taken during the routine simulation process which is part of the planning of radiotherapy treatment at the study site. During the simulation, fluoroscopy is performed and after the beam parameters and shielding information is confirmed by a radiation oncologist, hard copy images are printed out on size A4 plain paper. The simulation print outs are subject to a magnification factor and thus could not be used for this study. For this study, hard copy films were taken in the treatment position.

Simulator images were taken from right lateral side only for the purpose of this study. Radiographic cassettes fitted with standard intensifying screens were used as image recording media. The cassettes were loaded with blue sensitive screens. As a routine in the department, as part of the planning process, fluoroscopic simulation is done and hard copy simulated images printed on size A4 printing paper. For this study, the simulator images were obtained on hard copy films to be used as a standard against which four cobalt-60 treatment unit check films were compared. One simulator film was taken for each patient at the same source-to-skin (SSD) of 80cm (treatment distance at study site) distance and focus-film-distance (FFD) of 110cm for each patient to yield the same magnification factor as the four treatment unit checks films. The simulator films were processed using a conventional automatic film processor.

3.7.4 Acquisition of Treatment unit check films

During acquisition of treatment unit check films, the radiographic film was interposed between fogged and processed (completely darkened) radiographic films to prevent action of the intensifying screens on the unexposed film. This is due to high energy gamma radiation from the treatment unit and thus the intensifying action of the phosphor screens on the radiographic film is unnecessary. Treatment verification films were not available at the study site and thus the in-house experience was used to obtain treatment unit check films.

A single exposure was used to obtain treatment unit check films with details of treatment field and anatomical bony landmarks. The check films were taken after treatment parameters were set, before the treatment was given. An exposure time of 0.01 seconds was used to obtain the check films. The exposure time used was chosen,

as a result of the pilot study, to produce optimum film quality. One treatment unit check film was taken once a week for the first four weeks of radiation treatment. The radiation treatment check films were processed using a conventional automatic film processor.

The cobalt-60 therapy unit check films for each patient were taken at the same source-to-skin (SSD) of 80cm and focus-film-distance (FFD) of 110cm for each patient to yield the same magnification factor as the simulator film.

3.7.5 Data coding

For the purpose of data collection and accurate grouping of data, research assistants had all identification particulars of the participants. Letter and number coding of acquired data was used for each participant in order to safeguard their identity of the study participants. The researcher entrust qualified and respected staff members (R1 & R2) to collect and code the data. The coding followed a sequence of identification as P1, P2…P35; same for simulator film (SF) SFP1, SFP2…SFP35 and check films were coded as P1CF1, P1CF2, P1CF3 & P1CF4 which was done for all patient participants. The purpose of coding these data sets is to remove personal identification of research participants and research assistants as a way of ensuring confidentiality.

A set of data for each participant was then kept in an individual envelope handed to therapy radiographers treating patients and were kept under lock and key. No other person could access the data apart from the research assistants and the researcher.

3.7.6 Measurements

For each right lateral portal image, measurements were taken by a medical physicist designated as research assistant three (RA 3), from specific anatomical bony landmarks clearly identifiable on both the simulator film and Equinox treatment unit check films from the centre of the radiation treatment field. The specific bony landmarks used predominantly were the external auditory meatus, the nasal bridge, points on mandible, the clinoid processes of the pituitary fossa among others. The positions of the bony landmark were measured with respect to antero-posterior and supero-inferior directions in relation to the radiation field centre. Appendix XI indicates tabulated measured Simulator and Port image values. These measurements were entered into an SPSS version 18 statistical programme which is installed in a

private laptop accessible only to the researcher and the statistician appointed by the researcher. The data presented for analysis only contained number coding of participants and thus there was no way that one would identify the participant that data was derived from.

3.7.7 Data analysis

The measurements taken of all simulator and radiation treatment unit check films provided the data analysed in this study using mathematical methods as given by the RCR (2008) for reporting the results in terms of random and systematic errors. The equations for calculating random and systematic errors for individual patient and that of the population are given as:

Systematic Set-up errors

Equation 1: Individual mean set-up error

$$m_{individual} = \frac{\Delta_1+\Delta_2+\Delta_3+\Delta_4+\Delta_n}{n}$$

Where ($m_{individual}$) is the mean error for an individual patient calculated by summing the measured error for each imaged fraction ($\Delta_1+\Delta_2+\Delta_3+\Delta_4$) then dividing by the number of imaged fractions (n)

Equation 2: Overall population set-up error

$$Mpop = \frac{m_1+m_2+m_3+m_4+... + m_p}{P}$$

Where (M_{pop}) is the overall mean for the analysed patient group. The means for each individual patient ($m_1+m_2+ m_3\ldots$) being summed up and the total divided by the number of patients in the analysed group (P).

Equation 3: Population systematic error

$$\sum^2_{setup} = \frac{(m_1- Mpop)^2 + (m_2 - Mpop)^2 + (m_3- Mpop)^2+\ldots+ (m_n- Mpop)^2}{(P-1)}$$

Where the systematic error for the population ($\sum_{set-up}$) is defined as the standard deviation (SD) of the individual mean error about the overall population mean (M_{pop}). It is calculated by summing the squares of the differences between the overal population mean derived from equation 2 and each individual patient mean derived from equation 1.

Random set-up errors

Equation 4: Individual random error

$$\sigma^2_{individual} = \frac{(\Delta_1 - m)^2 + (\Delta_2 - m)^2 + (\Delta_3 - m)^2 + \ldots + (\Delta_3 - m)^2}{(n-1)}$$

$$\sigma_{individual} = \sqrt{\{ \frac{(\Delta_1 - m)^2 + (\Delta_2 - m)^2 + (\Delta_3 - m)^2 + \ldots + (\Delta_3 - m)^2}{(n-1)} \}}$$

This is the standard deviation SD of random errors ($\sigma_{individual}$) for each individual patient. It is calculated by summing the squares of the differences between the mean and set-up error from each image.

Equation 5: Population random error

$$\sigma_{setup} = \frac{\sigma_1 + \sigma_2 + \sigma_3 \ldots \sigma_p}{p}$$

The population random error ($\sigma_{set\text{-}up}$) is the mean of all the individual random errors ($\sigma_1, \sigma_2, \sigma_3, \ldots$) divided by the number of patients in the analysed group.

These five equations from The Royal College of Radiologists (2008) were used in this study in answer to sub question one (1) and sub question two (2).

3.7.8 Delineation of the research

This study was conducted in the radiation treatment department of the only state run hospital in Kenya with radiation treatment facilities. The other available radiation treatment centres are privately run. Patients confirmed to have cancer are referred from the entire country for radiation therapy at the hospital which is also the largest national teaching and referral hospital. Most cancer types are treated at the radiation therapy department but this study was conducted on patients with cancer of the nasopharynyx (NPC) also referred to as nasopharyngeal carcinoma and any other head and neck pathology treated using the same external beam radiation treatment technique. This study is limited to 35 participants, treated at one radiation oncology department, on one radiation treatment unit.

3.7.9 Assumptions

The following assumptions underlie the data collection and analysis procedures that were used in the study;

- Radiation therapists are trained and sufficiently experienced to provide quality treatment.

- The researcher-designed instrument validly measures what it purports to measure

3.8 Ethical Considerations

In order to fulfil the concern for ethical implications, as considered essential to the success and validity of any study by Wells (1998), ethical approval was granted by the Research Ethics Committee of Cape Peninsula University of Technology (Appendix X) and the Research and Ethics Committee of the study site (Appendix V). Furthermore approval to collect data was obtained from the head of department (Appendix VII) also at the study site. However, some changes had to be done as suggested and indicated (Appendix VI) by the Ethics and Research Committee at the study site. One of the concerns was the consent form (Appendix VIII) designed in English language which was required to be translated into Kiswahili (Appendix IX). Kiswahili is the most common language in Kenya, and considered as a national language, thus a consent form in the language is considered to enhance the understanding of the message in the consent information for the participants (Burns & Grove, 2003).

Patients enrolled for the study were protected based on the three fundamental principles on the human rights need to be protected in research (Brink et al, 2006:32-37; Leedy & Ormrod, 2005:101-102) which includes the right to: protection from discomfort and harm, fair selection and treatment, and privacy.

The researcher respected the right of the participants by:-

- Ensuring that all data collected during the study was protected from being divulged and participants' names were not revealed or used during data collection. Participants were identified by number coding and images generated during simulation and treatment unit check films coded as explained in section 3.7.5. This ensured that the right to privacy was secured by the researcher.

- Ensuring that informed consent (Appendix VIII) or (Appendix IX) was signed and dated by all participants.

- Those participants not willing to consent to be part of the study were respected and their decision did not affect the services rendered to them. No persons were forced to participate, and all took part willingly.

3.9 Position of Researcher in the study

The researcher is an employee of the national referral and teaching hospital in a senior therapy radiographer capacity with qualifications of Bachelor of Technology: Radiography (Therapy) and diploma in diagnostic radiography with seventeen years work experience. The researcher took an active role in this study as a primary researcher and provided necessary guidance to research assistants involved in this study.

Hicks (2004) points out that any research involving human subjects must be conducted by someone who has sufficient skills and competence to undertake the necessary procedures without inadvertently harming the subjects, either physically or psychologically. In addition, the researcher should have fundamental respect for the participants (Hicks, 2004). In this study, the researcher demonstrated respect for persons by protecting their rights as stated in section 3.9 and, during the entire research period, maintained responsibility to demonstrate respect for the scientific community by protecting the integrity of scientific knowledge in working closely with supervisors and staff that provided their expertise in the field (Burns & Grove, 2003). The researcher took responsibility in the choice of methodology that ensured use of scientific tools in an honest, responsible, open and ethically justifiable manner (Burns & Grove, 2003).

3.10 Minimising bias

Sica (2006) indicate that bias is not totally avoidable but that it can be minimized through careful planning at the study design stage. In order to minimize bias in this study, the researcher identified and acted upon the following in order not to limit the generalisability of the study:

3.10.1 Sample bias

Hicks (2004) cautions that a researcher is in a position of power and influence over research participants, thus the authority must never be abused in order to coerce patients into taking part in a study against their will. The sample bias can arise when the intended sample does not adequately reflect the spectrum of characteristics in the study population (Sica, 2006). In this study, this was avoided by describing the selection process as explained in section 3.4, 3.4.1 and 3.4.2. Since it is not possible

to study the entire population; the most appropriate study sample is one that closely reflects the characteristics of the population of interest (Leedy & Ormrod, 2010).

3.10.2 Measurement bias

Measurement bias reflects a discrepancy in measurements obtained from the simulator and treatment unit check films, and could arise from both subjective (due to human error) or a measuring tool. In this study, use of standard equipment and accessories were used and one medical physicist was tasked with the measurements on the images. The researcher postulates that the measurements taken by one individual will have same measure of accuracy because one observer will see one structure on all images from one participant in the same way thus minimising nonuniform measurement bias (Sica, 2006).

3.10.3 Use of research assistants

In this study, the researcher did not involve himself in recruitment and measurement of data but used research assistants hence the researcher did not have an influence in the selection of participants and the generation of numeric data in this study.

3.11 Validity in the study

The validity of a measurement is said to be the extent to which the instrument measures what it is supposed to measure (Leedy & Ormrod 2010). Standard measuring tools were used in this study as well as standard simulator and radiation treatment unit for all subjects, therefore, the results of this research are valid in that the same methodology and equipment would yield similar results as in this study. In order to ensure that the result of this study is generalisable to a whole population (Brink et al, 2006), external validity was considered in conducting the study at the only site providing radiation therapy in Kenya and enrolling all study participants who presented and met the enrolment criteria. The use of institutional documents to provide information such as participants' demographic and pathological information is considered by the researcher to enhance internal validity of the study since institutional documents are assumed to be true and consistent which indicate that the results of this study are a true reflection of the study.

3.12 Reliability

Reliability relates to the methods of data collected and the concern that they should be consistent and not distort the findings (Leedy & Ormrod 2010). Generally, it entails an evaluation of the methods and techniques used to collect and present the data (Denscombe, 2002). The researcher made use of a quantitative methodology which employ statistical method of calculation for the comparative measurements for agreement on the simulator and cobalt-60 images. The statistical method of calculating results are derived from a reputable publication and the use of SPSS and excel to illustrate data improves the reliability because the use of scientific methods will yield similar results, hence consistent findings (Mason, 2002).

The method and instruments used in data collection were the same for all patient participants. In the analysis process, the researcher chose a method that has been used by the Royal College of Radiologists (2008). It can therefore be deduced that the information available from the analysis is a true reflection of the study. The data that was obtained in the analysis process underwent the same coding process.

3.13 Research timeline

The following figure details work plan drawn by the researcher to schedule the study and ensure completion by the end of September 2012.

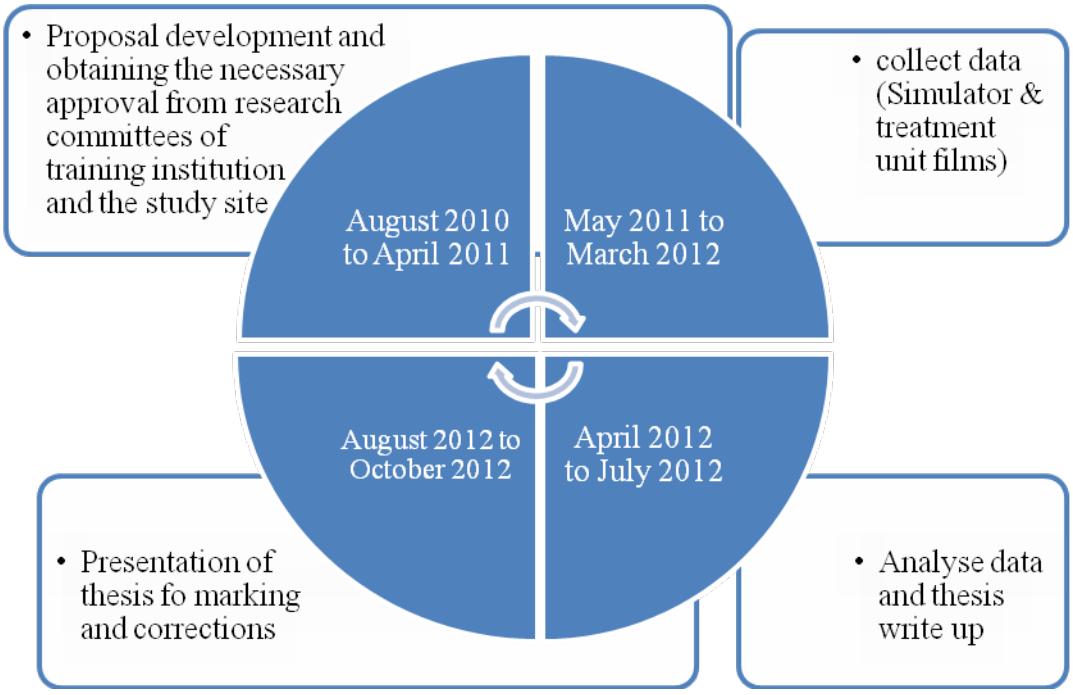

Figure 3.4: Summary of research timeline

3.14 Chapter conclusion

This chapter indicated the methodology applied to answer the research question using an appropriate quantitative study design that has been desribed. Ethical considerations were addressed and covered issues such as obtaining ethical approval from relevant authorities as well as obtaining informed consent from participants. In the next chapter, the results of the study conducted on 35 consenting participants are statistically presented using appropriate methods which give meaning to the collected and analysed data.

Chapter Four

Presentation of the results

4.1 Introduction

During the period 20th April 2011 and 4th May 2012, thirty-five (35) new patients meeting the enrolment criteria treated with external beam radiation therapy on Equinox cobalt -60 unit at a national teaching and referral hospital in Kenya were studied for random and systematic errors in radiation therapy beam alignment using portal imaging. All patients were treated with curative intent. In this chapter, the results of the prospective study are presented.

4.2 Patients' characteristics

4.2.1 Gender and age presentation

The study group comprised of 35 participants of whom 26 (74%) were males and 9 (26%) were females which gives a male to female ratio of 2.9:1. The mean age of the patients at the start of radiation treatment was 38 years, with a range of 18-75 years. The age mean by gender is calculated as being 40 years in males and 32 years in females. Figure 4.1 below is a pie chart on gender presentation of the study group.

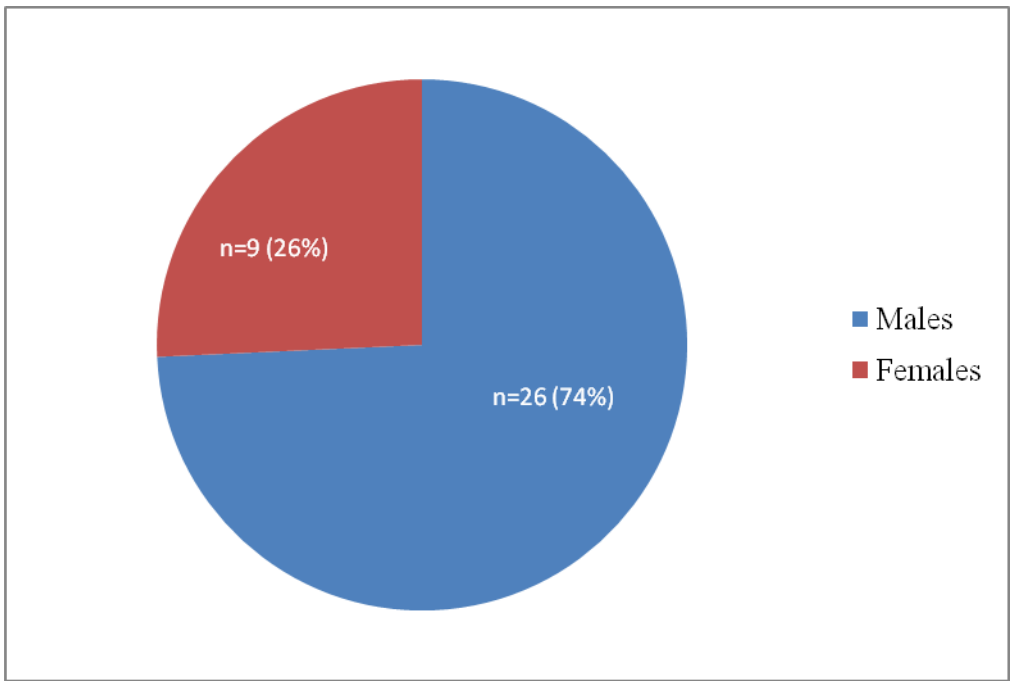

Figure 4.1: Study group gender presentation

4.2.2 Histopathological presentation

The patients presented with varied histological types of carcinomas which were as follows: nasopharyngeal carcinomas in (n=27) 77.1% of the patients, carcinoma of the paranasal sinuses in (n=7) 20%, followed by malignant non-Hodgkins lymphoma (n=1) 2.9%.

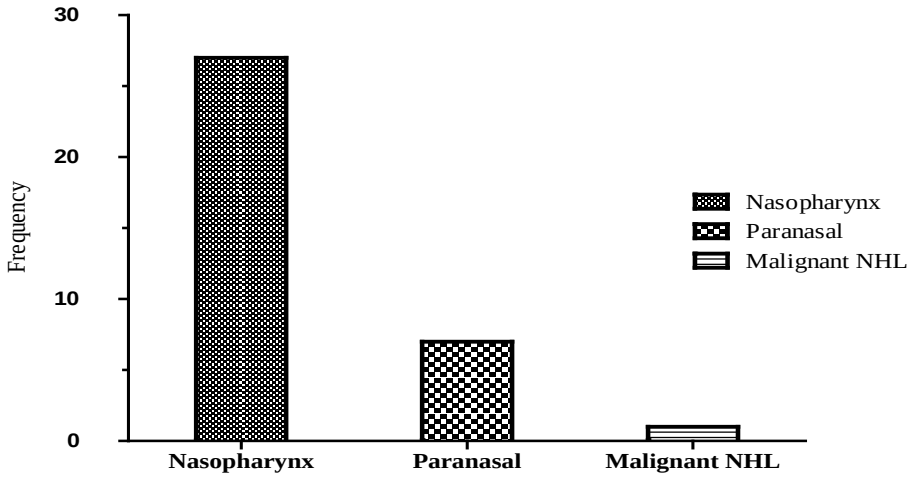

Figure 4.2: Site of occurrence of cancer

The most predominant carcinoma in the nasopharyngeal group was anaplastic (n=15) (55.6%), other histologic types (n=9) (33.3%) included squamous; non-keratinising; poorly differentiated; and angiosarcoma. Unspecified pathology was found in (n=3) 11.1% of patients. Figure 4.3 shows the patients' histopathology of nasopharyngeal carcinoma at presentation.

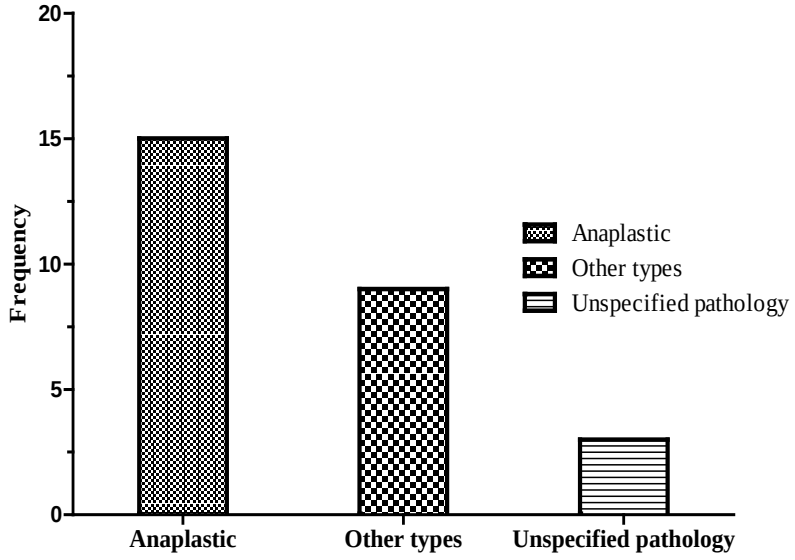

Figure 4.3: Nasopharyngeal carcinoma presentation

4.3 Tumour staging

The tumours were staged according to the TNM classification with the distribution presenting as follows: stage I (T1, N0) 0%, stage II (T2, N0) 0%, stage III (T2, N1) 17.1% and stage IV (T1-3 N2-3) 51.4% and T4 N0-1) 11.5%. For further analysis of the staging, the tumours are broadly divided into early tumours (T1-2 N0, or stage I & stage II) of which there were no cases in this study, (n=0; 0%) and advanced tumours (T1-2 N1-3, T3-4 N0-3, thus stage III & stage IV) 28 cases, 80%. The other 7 cases, 20% had unspecified pathology. Of the 22 patients with T4 disease, the majority (n=15) 68.2% had radiographic evidence of destruction of the base of the skull.

No patient (0%) was clinically N0 at the beginning of treatment. The detailed description of the patient staging is shown in Table 4.1 Below.

Table 4.1: Stage grouping of patient participants

Stage	**T**	**N**	**M**	**Total n**	**Total %**
Stage I	T1	N0	M0	0	0%
Stage II	T2	N0	M0	0	0%
Stage III	T3	N0	M0	0	0%
	T1	N1	M0	0	0%
	T2	N1	M0	6	17.1%
	T3	N1	M0	0	0%
Stage IV	T4	N0	M0	1	2.9%
	T4	N1	M0	3	8.6%
	Any T	N2	M0	8	22.8%
	Any T	N3	M0	10	28.6%
	Any T	Any N	M1	0	0%
Stage Unspecified				7	20%
Total				**n=35**	**100%**

4.4 Portal film study

During the data collection period (i.e April 2011 to May 2012), a quality assurance procedure was formulated to study radiation treatment field alignment errors by comparison of simulator image as a reference image with the images taken on Equinox cobalt-60 treatment unit. Thirty-five (35) patients who met the enrolment criteria were entered into the study, however, 3 of these patients were excluded from the portal film study data analysis as the data was not conclusively obtained for the following reasons: 1 patient died during the study period, 1 patient was rested from treatment due to treatment related side effects, and the third patient was exempted as a result of the data production deadline. In this section (section 4.4), the results of a cobalt-60 portal imaging study on 32 patients with nasopharyngeal carcinoma and any other head and neck carcinoma treated using the same radiation treatment technique as for nasopharyngeal carcinoma are presented.

4.4.1 Study results

A total of 160 images (32 simulation images and 128 cobalt-60 portal images) were obtained and analysed for accuracy (systematic) and reproducibility (random) in radiation beam alignment. These were achieved by doing the evaluation in two different comparisons termed as comparison 1for systematic errors and comparison 2 for random errors. GraphPad Prism 5 for windows version 5.04 was used to analyse the data that is presented.

Comparison 1: Simulator image and first portal image

This comparison was used to provide information regarding the accuracy (systematic errors) of radiation treatment by comparing the measurements taken on the simulator image to those measurements derived from the 1st portal image. Figure 4.4 below is a side by side comparison of absolute measurements on the simulator and the means of 1st cobalt-60 portal images as a result of a t-test. Table 4.2 gives comparative figures of the variations between the simulator and the means of the 1st portal images.

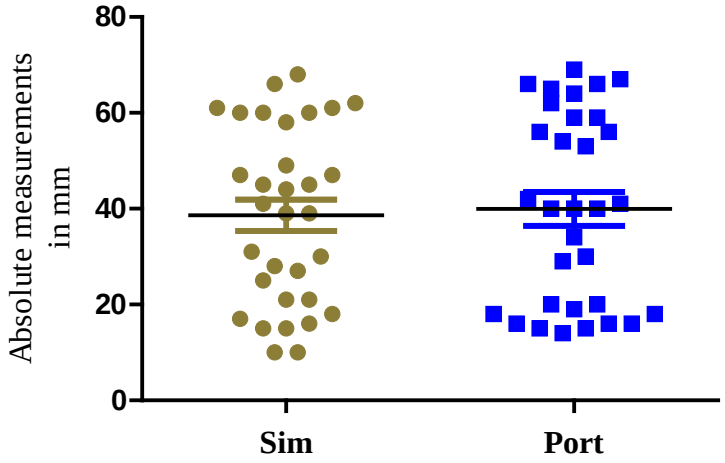

Figure 4.4: Systematic error histogram indicating absolute measurements in mm

Table 4.2: Simulator and 1st portal values comparison by t-test function

t-test results	*Simulator value*	*means of 1st Portal value*
25% Percentile	21	18.25
Median	40	40
75% Percentile	59.5	59
Maximum	68	69
Mean	38.63	39.97
Standard deviation	18.51	19.94
Standard error	3.272	3.526
Lower 95% CL	31.95	32.78
Upper 95% CL	45.30	47.16

The difference of the absolute measurements between the simulator values and the means of the 1st portal film values (which were used to plot figure 4.4 above) were calculated and used to plot figures 4.5 and 4.6 below. Figure 4.5 indicates the results of the comparison to be; median 4mm, mean 4.4mm, standard deviation 3.25 and a standard error of 0.575 for the study group. The difference between the simulator and the portal images of individual patients varied between no difference (0.0mm) as the minimum and 11mm as the maximum with the lower 95% CL of mean being 3.23mm, the upper 95% CL of mean being 5.58mm. The 25% percentile was 1.25 and the 75% percentile calculated to 7.75. Figure 4.5 indicates that the differences in measurements in 9 of the patients considerably skew the results as greater than from the tolerance level of 4mm.

Figure 4.6 gives a breakdown on the frequency distribution of the difference in simulator and the 1st portal film measurement given in millimeters. The histogram depicts that 37.5% (n=12) of the patient measurements were within 2mm, 56.25% (n=18) were within 4mm and 43.75% (n=14) indicated a difference greater than 4mm.

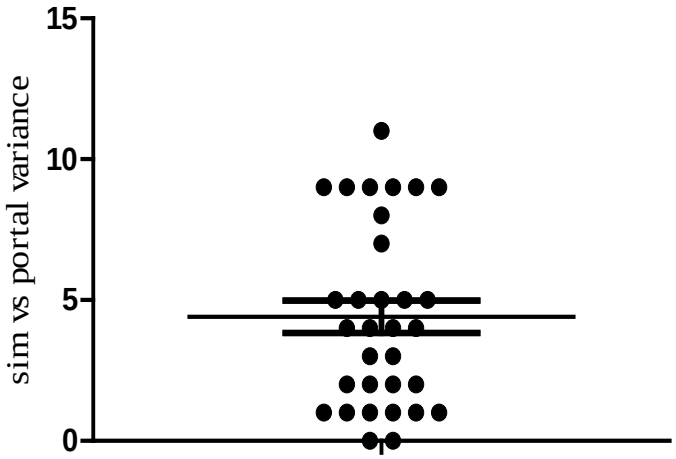

Figure 4.5: Systematic mean error histogram

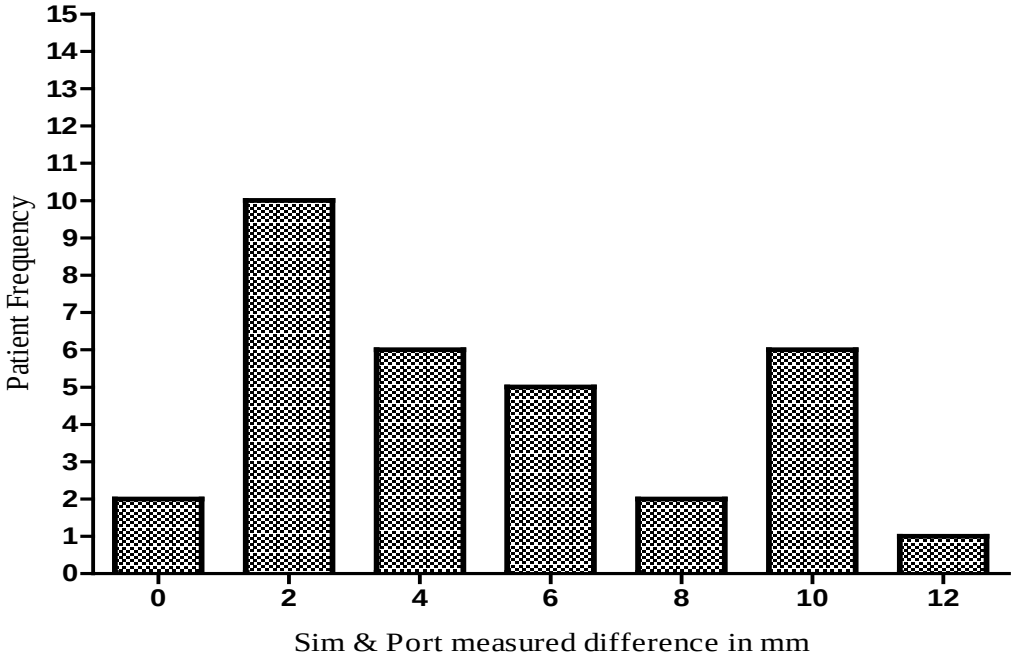

Figure 4.6: Systematic error frequency distribution histogram

A linear correlation analysis was performed which indicated no significant difference in the measurements between the simulator and the means of the 1st portal film measurements. Figure 4.7 is a presentation of the correlation. The means of the portal films are shown to be close to the trend line as described by the R^2 value. The R^2 value

describes the goodness of fit of the means of measurements of the 1st portal images to those of the absolute measurements on the simulator film. It calculated to an R^2 value of 0.9290. The goodness of fit varies between -1 to +1. According to NC university (2004), an R^2 value which is less than 0.1 in either the positive or negative direction is regarded as insignificant. This is in concurrence with personal information from Dr. Alistair Hunter (GSH, Radiobiology department) that the closer the R^2 value is to 1, the better the fit. This linear regression has demonstrated that the correlation between the simulator and 1st portal film comparison is not significant.

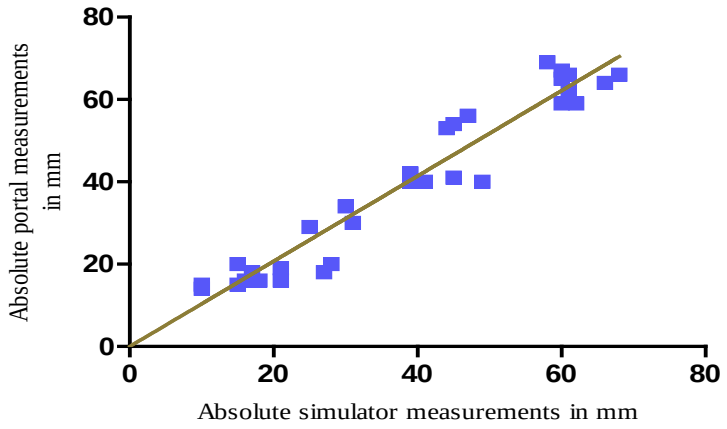

Figure 4.7: Linear regression histogram

Comparison 2: First portal image and subsequent three portal images

In this comparison, measurements derived from the first portal image were compared with the means of individual patient participant's subsequent three portal images. This was done to provide information regarding the reproducibility of radiation treatment. Table 4.3 below details the results of the comparative analysis.

The absolute measurements of the 1st portal and the means of the subsequent 3 portal values were plotted for linear correlation analysis. The results are presented in figure 4.8 below. The results calculated to an R^2 value of 0.9959 with a slope of 1.004 to 1.024 at 95% CL. Considering that an R^2 value which is less than 0.1 in either the positive or negative direction is regarded as insignificant (NC State University, 2004), the result of this comparison is much closer to 1 and thus a narrow slope which indicate close correlation between the comparison. This linear regression (Figure 4.8) and the calculated comparative analysis (Table 4.3) using GraphPad prism 6 software has demonstrated that the correlation between the simulator and 1st portal film comparison is not significant.

Table 4.3: Difference of 1st portal values and means of subsequent 3 portal values

Variable	*1st portal measured value*	*difference with portal means*
Minimum	13.75	-1.00
25% percentile	19.06	0.0
Median	41	0.5
75% percentile	60.44	1.250
Maximum	69.50	4.25
Mean	40.71	0.742
Std. Deviation	19.87	1.205
Std. Error of mean	3.513	0.213
Lower 95% CL of mean	33.55	0.3072
Upper 95% CL of mean	47.88	1.176

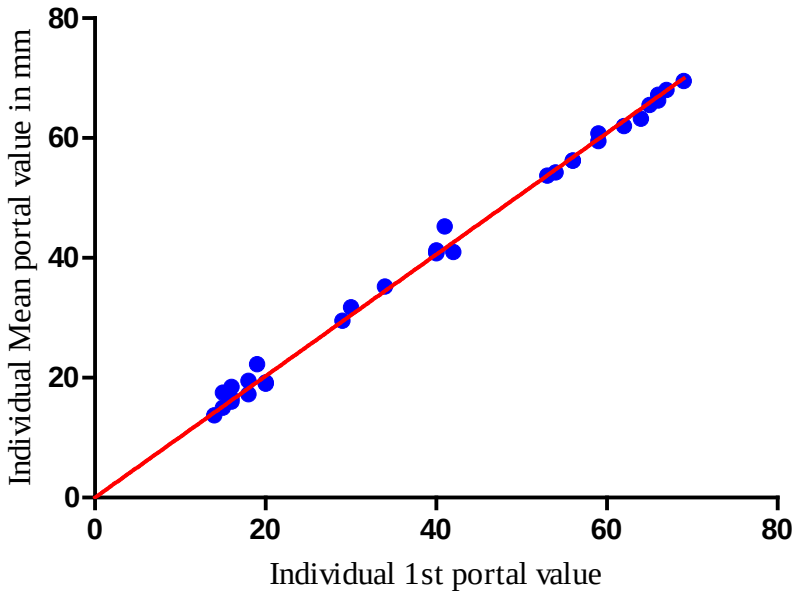

Figure 4.8: 1st portal value and individual mean portal value comparison

The absolute measurements of the 1st portal and the mean portal values were further normalized to 100% of the first portal image values as presented in figure 4.9 below in order to show the actual normalized % with standard deviation of each individual 1st portal and the mean portal value comparison. The height of each bar indicates the mean % normalized to 100% of the 1st portal while the vertical lines on the bars indicate the magnitude of the standard deviation in each of the participant. The figure indicate the minimum percentage to be 95% and the maximum percentage to be 117%

with a mean of 102.5% with the lower 95% CL of mean being 100.4% and the upper 95% CL of mean being 104.5%. The standard deviation calculated to 5.704, standard error of 1.008 with a minimum standard deviation of 0.0% and a maximum of 17.45%.

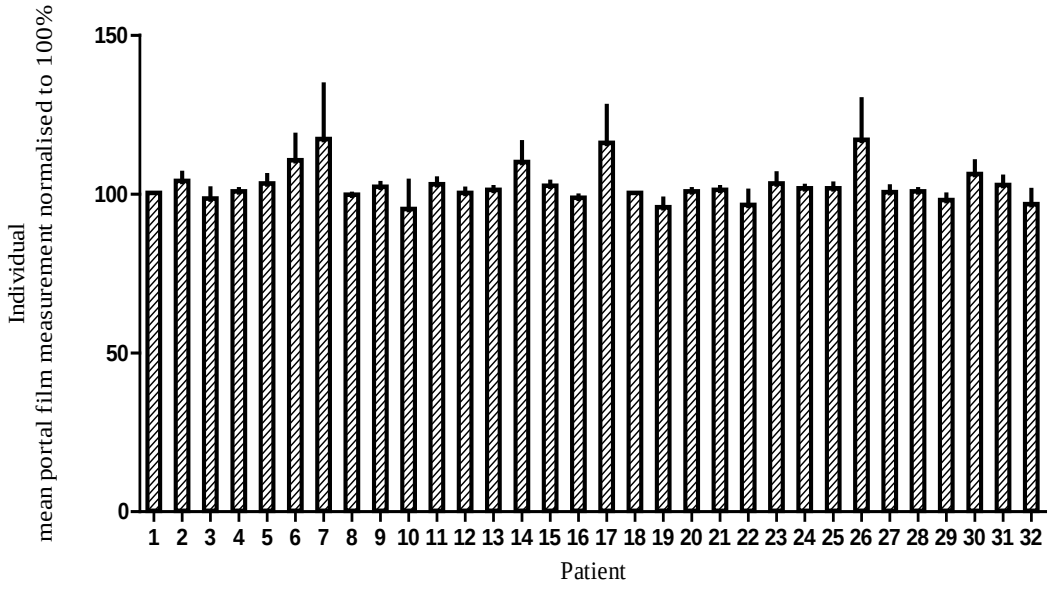

Figure 4.9: Individual random error histogram

This is further depicted in figure 4.10 which indicate that the majority of the % differences in measurements between the actual weekly portal % values normalized to 100% of 1st portal values were between 92-108% (colour band in figure 4.10). It is further depicted that some measurements in approximately 8 of the patients skewed the results outside the 92-108% band.

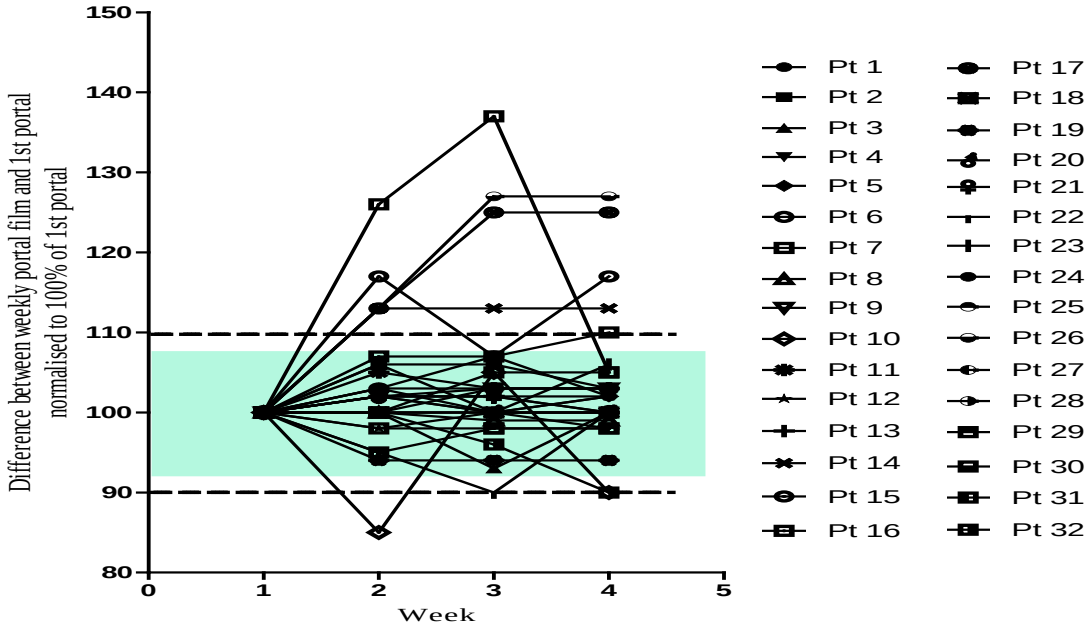

Figure 4.10: Normalised % difference between weekly portal films & 1st portal film

4.5 Conclusion

The results of a quantitative study on the accuracy and reproducibility of radiation treatment to patients in this study group has been presented. The results were categorized as followed: patient characteristics, histopathological presentation to include tumour staging and the portal film study. The next chapter is the concluding chapter which discusses the findings of the study and compares the findings with literature reviewed on the topic of portal imaging in nasopharyngeal carcinoma.

Chapter Five

Discussion, limitations, conclusion and recommendations

5.1 Introduction

The results of the study have been presented in the previous chapter. The current chapter discusses the results compared to the literature reviewed in this study and proposes recommendations postulated by the researcher to be necessary to improve treatment delivery to patients as in the study. The challenges and limitations of the study are given and an area for further research in the field of study is identified. Conclusions are drawn based on the findings of the study as they address each sub-question of the study.

5.2 Discussion

5.2.1 Patients' gender, age and pathologic characteristics

The study group presented with a high male to female ratio commensurate with previously reported literature at the study site by Clifford (1972) and globally by Jemal et al, (2011). This study group presented with a mean age of 38years, which is a tendency towards the lower range implying that nasopharyngeal carcinoma is currently presenting in younger patients at the study site compared to the earlier figures by Clifford (1972) of 50-54 years and that by Thompson (2007) of between 40 and 60 years. It is notable that the cancer presented at an advanced stage in the entire study group. This could be associated with the characteristic of nasopharyngeal carcinoma to be asymptomatic before development of a mass due to the anatomically inaccessible location (Razak et al., 2010; Spano et al., 2003) and only diagnosed upon appearance of a cervical mass (Thompson, 2007). The lack of prompt access to diagnostic and treatment facilities typical in developing countries such as the study site could have significantly contributed to late presentation of the cancer in this study group (WHO, 2008a; Sikora, 1999). It is not unusual for the patients in the study group to have been managed for other ailments before the cancer was diagnosed and this could contribute to the tumour progression. Thus late stage presentation occurs which limits curative treatment which then results to poor overall survival. The characteristics of the 7% in the study group whose information regarding tumour staging was unspecified could not be quantified, but the researcher is of the opinion that they could have presented at late stage.

The patients' gender, age and pathologic characteristics in this study is compared to one conducted in China by Yi, Gao and Huang et al. (2006) involving a large study group of 905 NPC patients. Table 5.1 indicates a high male to female ratio in both groups similar to other studies by Xu et al. (2010) and Thompson (2007) of about 3:1 irrespective of geographic location. The patients presented predominantly with late stage NPC in all the mentioned studies which is unfortunate for this group of patients for late stage presentation is associated with decrease in overall survival in 50-60% even with adequate treatment (Yi et al., 2006). The main cause of the decreased overall survival is reported as being local regional relapse and distant metastasis (Yi et al., 2006; Chow et al., 2002; Chua et al., 2001), especially for T4 and N3 patients (Chow et al., 2002; Cheng et al., 2001; Sham et al., 1990). T4 and N3 patients constituted 62.9% in the current study group (see section 4.2). Unspecified pathologies were reported by Yi et al. (2006) and by the researcher in the current study which indicate a break in the information regarding pathologic classification which has been documented to be necessary for it determines the selection of the appropriate treatment options and sequencing. Table 5.1 below is a comparison of some characteristics of patient participants in the Yi et al. (2006) study and the current study. The comparison indicates similarities of the variables in the studied groups irrespective of the magnitude of the difference in the number of patients in the two studies.

Table 5.1: Comparison of study group with that of Yi et a.l (2006)

Item	**Study group**		**Yi et al (2005)**	
	No.	%	No.	%
Total gender	35	100%	905	100%
Male	26	74%	669	73.9%
Female	9	26%	236	26%
Age in yrs	mean age 38		median age 48	
Clinical staging				
Stage I & II	0	0%	238	26.3%
Stage III & IV	28	80%	667	73.6%
Tumour classification				
Unclassified histology	7	20%	35	3.9%

5.2.2 Portal film study

The results of this study indicate the systematic and random errors to be within the reported ranges by Hurkmans et al. (2001) for the head and neck region of 1.6-4.6mm and 1.1-2.5 mm consecutively. The authors further mentioned that by following appropriate recommended procedures, the systematic and random radiation beam alignment errors can be reduced to less than 2 mm in head and neck patients and thereby improve clinical practice. Although the means of systematic and random errors of the current study group is within the reported range by Hurkmans et al. (2001) and by other authors such as Mileusnic (2005) and Huizenga et al. (1988), the 95% confidence of mean for the systematic errors was 5.58mm with 37.5% (n=12) of the patient measurements within 2mm, 56.25% (n=18) within 4mm and 43.75% (n=14) indicating a difference of more than 4mm. This implies that there is need at the study site to improve practice in order to reduce the magnitude of these errors.

In the second comparison which compared the measurements on the 1st portal image with the mean of measurements of the subsequent 3 portal images, the results indicated a close comparison. There was no difference in the 25% percentile of measurements, the median difference being 0.5mm, 75% percentile within 1.25mm while the maximum difference calculated to 4.25mm. The mean calculated to 0.742mm, standard deviation of 1.205mm with the upper 95% CL of mean being 1.176 while the lower 95% CL of mean was 0.3072mm. The results indicate that the second comparison which was used to provide part of the answer on reproducibility indicate a close comparison which indicate that the random component in the study was minimal.

The results of the prospective portal film study have indicated the range of systematic and random errors in radiation beam alignment that occur in the patients at the study site during the course of treatment. Although the population mean in this study was within the reported range of previous studies, the difference between the simulator and the 1st portal image of individual patients varied between no difference (0.0mm) as the minimum and 11mm as the maximum and 43.75% (n=14) had a difference of more than 4mm which considerably contributed to the systematic errors. Hurkmans et al. (2001) indicate treatment unit mechanical shortcomings, patient related, fixation related (immobilisation), and the accuracy with which RTTs are able to position the

patient to be sources of these errors. In this study, the researcher associates the following as possible sources of the observed results.

5.2.2.1 Immobilisation

A high degree of precision is required in the treatment of nasopharyngeal tumours due to the close proximity of critical structures such as the spinal cord, eyes and optic chiasm. Thus, all radical radiation treatments to this region need to be immobilised. Parker and Patrocinio (2005) indicate immobilisation devices to have two fundamental roles, these are; to immobilise the patient during radiation treatment; and to provide a reliable means of reproducing the patients' position from simulation to radiation treatment, and from one radiation treatment to another. In order to deliver precise radiation therapy to patients with nasopharyngeal cancers, patients must be treated in the same position that is technically comfortable and reproducible on each day of treatment. This minimises the risk of a geographical miss that may compromise tumour control and increase surrounding normal tissue damage. To help in this process, various immobilisation devices are available for immobilisation of the head and neck region. In this study group, it is indicated in section 3.8.1 that two different Orfit immobilisation materials (Orfit A & B) were used. Orfit material 'B' was reported to be too tight and unbearable for the majority (n=6 out of 10) 60% of patients immobilised using this material. This complaint was noted and pressure points were cut-out of the immobilisation material to enable some patient comfort during radiation treatment. Re-simulation was not done and no adjustments on beam alignment were done after the thermoplastic Orfit cut-out. The cut-out on the thermoplastic immobilisation material could have allowed some patient movement or misalignment even with the cast on. The researcher is of the opinion that this is the major cause of the errors observed. This is supported by literature (Tsai et al., 1999) that thermoplastic head mask has been shown to shrink 1.5 ± 0.3 mm in the first day after fabrication. There is evidence that even with the use of immobilisation devices, errors above 2mm have been reported in the head and neck region. A study by Hess et al. (1995) found an overall error of 3-5mm in a group of head and neck patients immobilised with Orfit masks. This implies that a meticulous immobilisation procedure using the right choice of Orfit material need to be observed at the study site in order to minimise errors as a result of immobilisation technique and materials.

5.2.2.2 Fixation related

Head and neck base-plates and thermoplastic Orfit materials are of varied number of fixation points. In this study group, it is noted from section 3.7.1 that a three point fixation head and neck base-plates and Orfit materials were used. These allow immobilisation of the head to the chin level with fixation points at the superior part of the cranium, right lateral, and left lateral face and does not include the neck where nodal involvement is observed in this group of patients.

It has been found (Rogues et al., 2005; Sharp et al., 2005) that immobilisation from the shoulder level, neck and head is essential to adequately achieve the level of accuracy required in the treatment of nasopharyngeal cancers and any other head and neck cancer. Further, Rogues et al. (2005) reports that shoulder fixation are critical in head and neck immobilisation allowing for a lower shoulder position, which enable lateral fields to extend inferiorly. The same author (Rogues et al., 2005) indicates that the lower shoulder position is suitable for off-cord electron beam positioning. For this reason, more than 3 fixation points would be required, a 5 point fixation point is reported to be commonly in use and allow for adequate stability to the head and neck region that would enable for radiation beam alignment of within 2mm.

Sharp et al. (2005) caution of the choice of immobilisation mask material for some are found to shrink and increase surface dose of radiation causing constriction and skin reaction (erythema). Sharp et al (2005) reported on a randomised trial with two different thermoplastic masks in 241 patients. The mask had to be cut out in some pressure points due to constriction in 15% of the patients. This implies that adequate consideration of the properties is essential in the choice of immobilisation material. Khan and Potish (1998) indicate that the material should hold its shape over the entire period of radiation therapy. Likewise, Van Lin et al. (2003) indicate that factors such as humidity, temperature, radiation, and change in patient anatomy due to weight loss or tumour factors should be taken into account especially with the choice devices that are to be used for long term radiation treatment.

5.2.2.3 Patient positioning

The use of Orfit immobilisation device on its own does not minimise radiation treatment errors. There is need for; the RTT to position the patient correctly in an individualised immobilization cast, and for the beam parameters to be accurately set on the treatment unit so as to minimize radiation beam alignment errors. This is achieved by ensuring that the RTT understand the method of immobilization and beam orientation being used for implementation of the planned radiation treatment and precisely follows the set-up instructions.

Patients that are immobilized with a thermoplastic mask are set up using marks placed on the immobilization cast which include table height alignment marks using lasers, central axis, radiation field centre, beam edges and shielding information to ensure that the daily set-ups are consistent and correct. Some radiation therapy departments have record-and-verifier computer system which helps ensure that the daily set-ups are consistent and correct by reading coordinates on the immobilisation cast. As part of the clinical requirements, set-up verification of treatment plans is done to confirm that the dose distributions will be delivered as planned so that random and systematic errors can be minimized and ensure patient safety.

Weekly portal film verification is done to verify that the patient is set up by the RTTs in the desired radiation treatment position. Additionally, a dose verification measurement may be performed on all radiation treatment fields using diodes to ensure that the radiation dose delivered by each beam is correct (IAEA, 2008).

5.2.2.4 Equipment mechanical shortcomings

Literature (AAPM TG 40, 1994; IAEA, 2005; IAEA, 2008) has shown the need to have both the simulator and the treatment unit alignment properties and geometry monitored in order to provide radiation delivery within the recommended value of 2mm. A typical example are the marks made on the immobilisation cast at the simulator which are used to realign the patient on the treatment unit using the identically positioned field light and positioning lasers. If there is misalignment of these parameters in either the simulator or the treatment unit, errors would arise (IAEA, 2005). In order to provide confidence in the accuracy and reproducibility of radiation delivery to patients, QA of equipment has been indicated to be a necessity. In

this study, it is evidenced by the appendices of the daily QA of the simulator and Equinox cobalt-60 which indicate measurements in agreement with recommended tolerance provided by the AAPM TG 40 (1994) which has been adopted by IAEA (2008). Furthermore, contract documentation at the study site indicates that both the Simulator and the Equinox cobalt-60 were still under warranty and that services were being provided by the supplier as stipulated in the contract documents available at the study site.

The simulator and the Equinox cobalt-60 at the study site are functional to the recommended standards of IAEA (2008) recommendations for quality provisions for radiation therapy service. The researcher is thus of the opinion that both the Simulator and the Equinox cobalt-60 were in good operational condition to provide quality in radiation beam alignment and would probably not have significantly contributed to the observed skewed part of the results in this study.

5.2.2.5 Patient related factors

The study group presented with stage 3 and stage 4 disease which is characterised with neck node involvement and as was pointed out in chapter four, no patient was clinically N0 at presentation. These patients can have the feeling of discomfort as a result of tumour bulk and thus can be restless when immobilised in the thermoplastic Orfit immobilisation device. This could be further aggravated by side effects of the radiation treatment which could make the immobilisation process a painful procedure for the patient. Thus, the patient may be unable to tolerate a treatment time slot of approximately 15 minutes when positioned in an immobilisation device.

In practice, the patient would communicate to RTTs how it feels when the immobilisation device is not consistent with previous set-ups. RTTs treating patients in this study group reported some patients being claustrophobic, especially in the group treated using immobilisation device B which was reported by patients to be constricting and thus unbearable. Although RTTs are aware and skilled in the preparation of these Orfit immobilisation casts, other factors like the long waiting time before commencement of radiation treatment when immobilisation device has already been made could result to the consequent tightness of the cast possibly as a result of disease progression. The immobilisation procedure can therefore be distressing to the patient and the patient can mistakenly be thought to be uncooperative, when in fact the patient is in a feeling of being trapped (Faithfull & Wells, 2003). Conversely, tumour

shrinkage happens during radiation treatment which could result in the loose fit of the immobilisation material and allow some patient mobility in the immobilisation cast. This is in practice noted by RTTs during treatment and would refer the patient for review at radiotherapy clinic. Patients under treatment at the study site are routinely reviewed weekly. It is at the review clinic that decisions are made regarding preplanning at the discretion of the reviewing radiation oncology consultant.

Rogues et al. (2005) indicate that a new mask is made in such patients whose tumour shrinkage or due to patient weight loss have rendered the initial immobilisation cast ineffective. The researcher did not observe any new immobilisation cast being made or patients being re-planned during radiation treatment in the study group but found it necessary to point out as one of the factors to consider as essential to minimising the beam alignment errors in patients as described in this section.

5.3 Limitations of the study

5.3.1 Radiation treatment planning and delivery technique

All patients were treated with Equinox cobalt-60 unit using individually shaped fields, as a routine two lateral parallel opposed fields at times with an additional anterior nasal field, depending on tumour extent to the nasal area, to ensure adequate tumour coverage. The dose was calculated at the midplane in nasopharynx with treatment planning based primarily on simulation images due to limitations in treatment planning tools (see section 1.13.1). With this radiation treatment planning technique, target location is based on information from physical examination, diagnostic imaging and surgical reports. Radiation beam direction and shapes are then selected with the aid of bony landmarks by use of a simulator (Chan et al., 2002). An established beam arrangement technique is commonly used (see section 2.4.1) and is based on the extent of the cancer. This radiation treatment planning technique has limitations, there is inadequate anatomy available, other than bony anatomy on the radiograph, to design treatment portals (Ching, 2009; Chan et al., 2002).

Problem with this radiation treatment technique

NPC is reported to present with unique local spread patterns particularly posterior extension and lateral extension into parapharyngeal space and superiorly through the skull base foramina (Waldron et al., 2003). This pattern of spread present a geometric dilemma such that shielding introduced into lateral radiation beams to protect critical

structures may also protect tumour resulting in under dosage (Waldron et al., 2003). The lack of appreciations of target volume and real volume of normal tissue in the treatment volume in three dimensions may lead to incomplete tumour volume coverage or excessive irradiation of normal tissue (Ching, 2009; Waldron et al., 2003). Furthermore, assessment of the delivered dose is only possible based on a single plane, conventionally the mid-plane (Waldron et al., 2003).

The failure of dose computation throughout the target volume is documented by Waldron et al. (2003) to possibly lead to inability to identify and correct dose inhomogeneities in target volume due to differing body contour and organ composition. Further, the radiation dose achievable with the use of cobalt-60 without electron beam availability, as at the study site, to boost nodal neck region is another major limitation to the amount of radiation delivery to approximately 66Gy. Yi et al. (2006) and Yan et al. (1990) have indicated the need for dose escalation to residual nodes in the neck which is typical of patients presenting with late stage disease such as in the study group.

The radiation treatment of nasopharyngeal carcinoma is documented to have improved overall survival in patients to a considerable extent especially with conformal radiation treatment techniques like 3DCRT and IMRT either with or without chemotherapy. This study has also indicated that escalated radiation doses to the primary lesion and involved regional lymph nodes improve the treatment results in terms of local control, overall survival, and disease free survival to patients with NPC.

5.3.2 Logistical limitations

The study was conducted at a time that the Equinox cobalt-60 had just been installed and commissioned. RTTs were therefore still not quite acquainted with the operations of the unit which implies that some radiation treatment procedures were taking more time than the treatment time slot of 15mins allocated at the study site for treatment of each patient. Additionally, processing facilities were not available at the radiation oncology department and processing of simulation and cobalt-60 films had to be done in the radiology department located approximately 250m away. Although the RTTs were accommodating during the research period, the researcher observed that occasionally, the processing of films were delayed at times till the next day as there were many patients waiting for their treatment. The installation, testing and

commissioning of the new Equinox cobalt-60 treatment unit resulted in treatment delays and thus there was a waiting backlog at the treatment site. The portal imaging of the study being not a routine procedure could have, as viewed by the researcher, exerted some pressure to the already busy RTTs.

5.3.3 Quality of portal films

Portal films have been indicated to be of poor quality (Hurkmans et al., 2001) and thus prone to a large error when manual measurements are conducted (Perera et al., 1999). Perera et al. (1999) document that differences of approximately 5mm have been associated to this method of measurement due to unclear reference bony landmarks which could introduce subjectivity bias by an observer, which in this study would be the research assistant 3 who did the measurements. Some authors have indicated the use of Kv imaging instead of portal imaging probably due to the reputation that reflect poor image quality that portal images have acquired. The poor quality in high energy portal film imaging as observed in this study could have been as a result of: poor contrast due to predominance of Compton scattering which takes place at megavoltage energies; image degradation due to scattered photons and secondary electrons, which cannot easily be removed; beam edge unsharpness of cobalt-60 beam which makes it difficult to determine the field edge in relation to bony anatomy; and the use of inadequate technique for example improper exposure or use of a wrong radiographic cassette for example a cassette with inadequate thickness of the front screen which allow electrons exiting from the patient a sufficient range to reach the film (AAPM TG 28, 1987). Besides poor image quality of the port films in this study, other geometric conditions which could have contributed to observed variation in simulator and portal film comparison are differences in magnification which could arise due to incorrect film positioning. Although the researcher designed a study protocol for the acquisition of the simulator and port films, it is acknowledged (Van de Geijn, Harrington & Fraass, 1982) that such mistakes can happen and affect the results of the comparison.

5.4 Challenges faced by the researcher

Some of the challenges encountered by the researcher during the research process were: timely feedback from Research Ethics Committee, positionality of the researcher, and difficulties in accessing library facilities.

5.4.1 Lack of prior knowledge on requirements for conducting research

The researcher had to submit the research proposal to the study site Research and Ethics committee. This Research and Ethics committee has criteria for submission of research proposal. In addition, the research proposal had also to be assessed by the educational institution's Faculty Research Ethics Committee. The involvement of two different committees ended up in a lengthy process which needs to be factored in the planning of the research. The writing of the proposal to suit the different requirements for submission by the two Research ethics Committees, and the waiting for response from reviewers was challenging and equally stressful to the first time researcher.

5.4.2 Positionality of the researcher

The researcher is an employee of the national referral and teaching hospital in a senior therapy radiographer capacity which imply that the researcher had to perform his daily duties as programmed at the study site. This meant that the researcher was under the operational requirements of the teaching and clinical practice of the study site, thus did not have control of such issues like booking of patients in the study group, equipment breakdown and prompt repairs among others. In addition, he took the role of a principal researcher in this study and provided necessary guidance to research assistants involved in this study.

Hicks (2004) cautions of direct participation by the principal researcher so as not to control the data collection process. The principal researcher thus had to entrust research assistance in data collection and production and the challenge was retaining an observer status while on the other hand ensuring that the research assistants and patient participants were relaxed and sufficiently informed about the requirements of the study.

A further challenge was choosing a methodology that ensured use of scientific tools in an honest, responsible, open and ethically justifiable manner (Burns & Grove, 2003). The researcher thus demonstrated respect for persons by protecting their rights as stated in section 3.9 and, during the entire research period, maintained responsibility to demonstrate respect for the scientific community by protecting the integrity of

scientific knowledge in working closely with supervisors and staff that provided their expertise in the field. The researcher also developed study procedures as described in appendices III and IV in order to generate numeric data that would answer the study concerns while limiting research bias.

5.5 Recommendations

Based on the findings of this study and the literature reviewed, the researcher recommends the following in order to improve practice of radiation treatment to the nasopharynyx and any other head and neck patient treated using the nasopharynx technique at the study site. In addition, some of the recommendations include procedures to quantify, report, and reduce radiation beam alignment errors to this group of patients.

5.5.1 Improved head and neck immobilisation

A range of head and neck immobilisation devices are commercially available for the immobilisation of head and neck region. Some departments use in-house constructed head and neck immobilisation devices. It is documented (Khan & Potish, 1998) that the immobilisation device, whether commercially acquired or in-house constructed, should conform to the patient's external surface contours. In order to provide adequate immobilisation for reproducible set-up and thus achieve recommended beam alignment without causing pressure on the patient, the researcher in this study recommend a non-shrink material, like Orfit immobilisation material A which was used in this study. In addition, the base-plate and Orfit thermoplastic material should enable for 5 fixation points in order to achieve the recommended immobilisation of within 2mm for the head and neck region. Khan & Potish (1998) indicate that the immobilisation material should be radio-transparent and be possible to cut away sections if necessary. A 5 point base-plate and 5 point Orfit thermoplastic materials are recommended by the researcher in this study for use at the study site, this should therefore be budgeted for.

5.5.2 Improved research interaction between role players

Sufficient interaction between university research departments and the radiation oncology clinical settings need to be encouraged so that timely assistance and prompt response is available to researchers. The researcher suggests that attention should be

given towards the identification of research problems in various areas of the profession which are of immediate concern both to the training institutions and clinical settings for better and realistic research. There is therefore the need for developing satisfactory liaison between the university authorities and clinical oncology departments so that academics can get ideas from professionals in clinical settings, for example consultants, medical physicist, RTTs and nurses on what needs to be researched. This in turn will be acceptable to practitioners and thus applied.

5.5.3 Introduction of new treatment modality and treatment planning and delivery

Unfortunately, conformal radiation therapy is unavailable at the study sites which compromise the amount of radiation achievable with the use of cobalt-60 without the advantage of 3DCRT planning tools and equipment with electron capability. The use of cobalt-60 enables the attainment of approximately 60-66Gy, while the study has shown that these patients require higher radiation dose in order to maximize the advantage of dose escalation to patients with nasopharyngeal cancer, especially the late stage presentation which was typical in the entire study group. There is need therefore, to plan for availability of 3DCRT planning tools which would include a dedicated CT scanner and treatment planning computer planning system. The department should in addition plan on the introduction of newer treatment modalities. A linear accelerator of 6-8MV x-rays and a range of electrons would be most appropriate for this study group, and in addition would be advantageous to other patients with cancers at sites such as breast and limbs.

5.5.4 Implementation of portal imaging protocols

Before this study radiation treatment accuracy and reproducibility had not been quantified as there was a lack of portal imaging. Hurkmans et al. (2001), among others, have indicated the need to have portal imaging at minimum on a weekly basis in order to monitor and reduce radiation beam delivery errors. The researcher recommend adoption of weekly portal imaging to all patients with nasopharyngeal carcinoma and other head and neck cancers while immobilised in the appropriate head and neck immobilisation Orfit mask as mentioned in the first recommendation of this section.

Guidelines should be developed at the study site indicating when the port films need to be taken and the action to be taken for port films whose measurements are out of tolerance. The researcher suggests depiction of these guidelines in a flow diagram

format and with adoption of better immobilisation materials and technique, the researcher suggests that the tolerance can be reduced to approximately 2.5mm. This has been found to be possible by Suter et al. (2000). If adjustment in beam alignment is made, it is important to verify it again by portal imaging to confirm if the change in the procedure has led to an improved treatment set-up. The researcher also recommends development and adoption of a simple correction protocol to be applied on a routine basis by RTTs.

5.5.5 Improvement of quality of portal films

It is documented (Droege & Stefanakos, 1985) that a technique chart consisting of tabulated values of exposure parameters for each radiation treatment site is useful in producing suitable optical densities in radiographic images. Development of technique charts for simulator and portal films are therefore recommended for the study site.

It is also acknowledged by the researcher that the film screen combination used in the study group could have contributed to poor portal images. AAPM TG 28 (1987) recommends the use of a 1 mm copper front screen cassette when using cobalt-60 radiation beam in order to obtain optimum quality high energy radiographs. The authors (AAPM TG 28, 1987) further indicate that the recommended cassette screen system is strong and thus avoid degradation through bowing, warping, screen damage (e.g. scratching) and loose hinges thus would be beneficial to the study site for it can be used for a considerable long time.

The researcher recommends planning for acquisition of such cassette screen system at the study site so as to improve the quality of portal films. In addition, Van de Geijn et al. (1982) advocates for the use of a graticule (reticule) which project a precise scale on the simulator and portal image and thus used as a common reference frame. The researcher is of the opinion that this device would have been meaningful in this study and therefore recommends planning for acquisition of the same.

5.5.6 Ongoing skills development and formal training of RTT

It is recommended by the researcher that ongoing training of RTTs be part of routine at the study site in order to improve their skills to make immobilisation devices and to position the patient according to the treatment plan. Portal imaging has been suggested (Suter et al., 2000) as one of the areas for role extension for RTT, and that RTT can competently make decisions regarding corrections as a result of inspection of portal

imaging with additional training. Suter et al. (2000) further indicate that RTT were much more efficient as a result of taking on the additional responsibility. The role extension eliminates the need to trace Radiation Oncologists to review portal images. This supports an earlier documentation by Swinburne (1971) that role extension into areas within the clinical domain would improve job satisfaction. In addition, the researcher suggests adoption of weekly film reviews as suggested by Fogarty et al. (2001) and Suter et al. (2000) with participation of RTT. This weekly portal review is seen by the researcher as an in-house learning activity and if adopted, the practice and quality of portal imaging will improve because everyone involved knows that the portal films will be viewed by other staff members and therefore improved treatment delivery to patients.

Formal training of RTT is also needed to support expansions of radiotherapy provisions in Kenya. This need has been recognised and with assistance from IAEA, the first group of RTT training is ongoing in Kenya. As the training is still in the formative stage, Barton et al. (2006) indicate of the need to facilitate knowledge transfer and support from developed countries especially in areas of protocols and for planning of service development. Through the input from Kenya government and IAEA, this has been provided by South Africa in terms of training and expert missions. Regional centre links have been recommended by Barton et al. (2006) for the reason that the types and stages of cases would be similar and treatment techniques more applicable. With support, the researcher is of the opinion that the RTT training in Kenya can serve the RTT training needs of the countries in East Africa.

5.6 Addressing the research sub-questions

The researcher asked three sub-questions which the study needed to address. These sub-questions were derived as a result of the observation by the researcher, of the lack of QC on portal imaging at the study site. This study site has not previously quantified the accuracy and reproducibility of radiation treatment to patients with nasopharyngeal cancer and other head and neck cancer which fall within the enrolment criteria. The three sub-questions therefore asked by the researcher were:

1. How accurate is the treatment field placement on Equinox cobalt-60 radiation therapy unit?

2. How reproducible is the treatment set-up during the period of radiation therapy using the cobalt-60 unit?

3. What are the recommended QC processes that ensure radiation therapy is accurate and reproducible on a cobalt unit?

In order to provide answers to the three sub-questions, a quality assurance study was formulated and carried out by the researcher and his research assistants which involved the taking of simulator and portal images on a defined study group. The researcher also reviewed literature on QA and QC of cobalt-60 and patient specific portal imaging. In answering question 1 and question 2, the researcher used an empirical method described by RCR (2008) for calculating random and systematic errors in radiation beam alignment. The results have been presented in chapter 4 and discussed in chapter 5. The researcher highlights the results specifically of the systematic nature that were observed to be in the higher range in 43.75% (n=14) of the study population whose results indicated a difference greater than 4mm. The researcher has associated the observed results to the use of immobilisation materials and technique and has provided recommendations that would allow for reduction of the errors to within 2mm.

For the purpose of this study, the accuracy is answered by the calculation for deriving systematic errors in radiation beam alignment. Reproducibility was answered by the comparison of measurements on the first portal image and the subsequent 3 portal images. The researcher notes that the results of the calculation that provide for an answer to reproducibility of treatment for this study group falls within the provided results for the random error component. The method used by the researcher to calculate for reproducibility by comparing measurements of the 1st portal image and the means of the subsequent 3 portal images were designed specifically for study purposes. The study group population random error calculated to 1.16mm using the RCR (2008) empirical method while the portal comparisons using researcher method calculated to a random population mean of 1.08mm. In the RCR (2008) method, the means of the measurements derived from the 4 portal images were compared with the simulator measurements. The researchers' method does not factor in the errors in the first portal image which could thus explain the difference in the means.

In answer to sub-question 3, the researcher reviewed literature on QA and QC requirements for both cobalt-60 radiation therapy equipment and patient portal imaging QA and QC. It was found in literature provided by experts in the field of medical physics which include AAPM TG 40 (1994); Thwaites et al. (2005); CAPCA, (2007); IAEA, (2008) among others, that periodic QA of equipment need to be in

place and evidenced with QC documentation. All these authors indicate an agreement in beam alignment in the head and neck region as for NPC to be within 2mm with the use of good immobilisation materials and beam delivery techniques. At the study site, it is evidenced by the appendices of simulator and Equinox cobalt-60 daily checks and contract documents at the study site that both the simulator and the Cobalt-60 unit were in good operational condition to provide quality in beam alignment to the recommended 2mm. The researcher has explored possible reasons for the observed results and has given recommendations backed with literature. The researcher is of the opinion that these recommendations, if taken into account, should improve the practice of radiation treatment to patients at the study site which thus reflect as benefit to patients in terms of accurate delivery of radiation dose to target volume and limiting dose to normal tissues.

5.7 Recommended areas for further research

The findings of this study has indicated that nearly all of the patients at the study site presented with late stage disease which Yi et al. (2006) and Yan et al. (1988) have indicate the need to have high doses given to this late stage presentation. The doses achievable at the study site are shown to be lower than suggested by literature for stage 3 and 4 which was observed at the study site. Limitation to the doses achievable at the study site is attributed to the lack of tools required for 3DCRT planning and delivery of radiation therapy to patients. Research on patients treated at the study site would provide valuable information regarding survival of these patients in terms of local regional control of disease, and overall survival after radiation therapy. Documented review of these patients for a period of 10 years would yield information that would be comparable to previously reported studies on the same cancer of the nasopharynx.

Another area for future research as viewed by the researcher is in the area of dose delivered to this group of patients by use of diode measurements to compare with the calculated dose.

5.8 Conclusion

This prospective study has shown the probable range of systematic and random errors that occur in beam alignment during the course of radiation treatment to patients treated using the same radiation treatment technique to the nasopharyngeal area at the study site. The study, as viewed by the researcher, being the only one on the subject of

portal imaging at the study site has built up a documented basis for the accuracy and reproducibility achieved in the treatment delivery to patients to this group of patients. In order to ensure that radiation treatment is delivered as planned, there is need to develop and adopt portal imaging on a routine basis in order to monitor, document and allow for mechanism to correct observed errors through portal imaging QA and QC. Hurkmans et al. (2000) indicate the need to establish a specific QA protocol to monitor both equipment and practice of treatment delivery at a regular, defined threshold and frequency.

Portal imaging to measure set-up errors is a standard practice in a large number of institutions and has made it possible to detect and reduce set-up errors for a large number of patients (Hurkmans et al., 2000). The set-up accuracy achievable with the availability of good immobilization is 2mm for the head and neck region. Late radiation treatment complications as a result of errors arising due to incorrect beam alignment can have a sever effect on the quality of life in patients treated with radiation to the head and neck region. The results of this study has shown the disparity of the delivered treatment from the planned, as a result of beam alignment errors, which indicate that certain measures need to be put in place at the study site in order to limit these errors to within recommended parameters. Literature (Hurkmans et al., 2000; Mileusnic, 2005; Khan & Potish, 1998) have indicated that misalignment exceeding the stipulated tolerance could result in patients receiving higher than planned radiation dose to normal tissues or lower radiation to target region with resultant serious consequences.

This study has also reviewed literature (Begnozzi et al., 2009; Hurkmans et al., 2001; Torgil, 1996) which has indicated 3DCRT as a standard method of radiation treatment delivery in the head and neck region and IMRT to be an advanced method of 3DCRT. For conformal radiation therapy to be successful with its tighter margins, the study has indicated the importance of accuracy in patient positioning, relative to the radiation beam; and using appropriate immobilization devices in order to minimize beam alignment errors. This study has demonstrated that beam alignment errors can be of concern since it has been documented by a number of authors which include RCR, (2008); IAEA, (2003); Thwaites et al., (2005) to be a major source of errors in radiation dose delivery.

This study has confirmed that the observed variations were considerably outside the limits of international standards in terms of systematic errors. These errors compromise the quality of treatments delivered at the study site. Recommendations have been provided and the researcher is of the view that if the recommendations are taken into consideration, the observed errors would be minimized to within the recommended 2mm.

Appendix I: Quality assurance programme for cobalt-60 unit

AAPM TG 40 Quality assurance programme for cobalt-60 unit

Frequency	Procedure	Action level
Daily	Door interlock	Functional
	Radiation room monitor	Functional
	Audiovisual monitor	Functional
	Lasers	2 mm
	Distance indicator	2 mm
Weekly	Check of source position	3 mm
Monthly	Output constancy	2%
	Light/radiation field coincidence	3 mm
	Field size indicator	2 mm
	Gantry & collimator indicator	1^0
	Cross hair centring	1 mm
	Latching of wedge & trays	Functional
	Emergency off	Functional
	Wedge interlocks	Functional
Annually	Output constancy	2%
	Field size dependence of output constancy	2%
	Central axis dosimetry parameter constancy	2%
	Accessories transmission factor constancy	2%
	Wedge transmission factor constancy	2%
	Output constancy versus gantry angle	2%
	Beam uniformity with gantry angle	3%
	Manufacturer's safety interlocks procedures	Functional
	Collimator rotation isocentre	2mm diameter
	Gantry rotation isocentre	2mm diameter
	Table rotation isocentre	2mm diameter
	Coincidence of collimator, gantry & table axis with isocentre	2mm diameter
	Coincidence of the radiation and Mechanical isocentre	2mm diameter

Appendix II: Daily QA of Equinox Co-60 unit

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KENYATTA NATIONAL HOSPITAL
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NAIROBI

REF: KNH/CTC/PHYS/DQA-Cobalt DATE: W.e.f May/2011

DAILY QA/QC MEASUREMENTS FOR COBALT 60 UNITS

TYPE OF CO-60 UNIT..Equinox Co-60..

TEST	MON	TUES	WED	THUR	FRI
DATE	6/6/2011	7/6/2011	8/6/2011	9/6/2011	10/6/11
1. Door Interlocks	Functional ☑ Notfunctional ☐	Functional ☑ Notfunctional ☐	Functional ☑ Notfunctional ☐	Functional ☑ Notfunctional ☐	Functional ☑ Notfunctional ☐
2. Radiation room monitor	Functional ☑ Notfunctional ☐	Functional ☑ Notfunctional ☐	Functional ☑ Notfunctional ☐	Functional ☑ Notfunctional ☐	Functional ☑ Notfunctional ☐
3. Lasers	2cm mm	2c mm	2 mm	2.0 mm	2c mm
4. Distance Indicator	OK mm	OK mm	OK 0.5 mm	OK 0.5 mm	OK 0.5 mm
5. Audiovisual Monitor	Functional ☑ Notfunctional ☐	Functional ☑ Notfunctional ☐	Functional ☑ Notfunctional ☐	Functional ☑ Notfunctional ☐	Functional ☑ Notfunctional ☐
Name: Designation: Signature:	E.OKoko med.phy	E.okoko med.phy	E.okoko med.phy	E.okoko med.phy	E.okoko med.phy

Appendix III: Immobilisation and Simulation study protocol

- Position the patient supine on simulator couch and select a head rest that fits under the patient's head and neck area, allowing the patient to lie comfortably on the simulator couch
- Align the patient in the desired treatment position using alignment lasers fitted within the simulator room with an agreed degree of flexion or extension of the neck as agreed with the prescribing radiation oncologist
- Warm and mould the orfit material to the patient's contour on the face and neck and secure the moulded orfit to the desired head and neck base-plate
- Using CT information, perform fluoroscopy using the simulator at a source to surface of the patient distance kept constant at 80cm for all patients
- Using lead wires, the radiation Oncologist should identify and indicate organs at risk that need to be shielded during simulation with respect to anatomical landmarks visible on the simulator image
- Mark position of the centre of radiation treatment beam to include beam angulations and field limits as determined with respect to anatomical landmarks visible on fluoroscopy screen of the simulator
- Mark a single cross axis patient contour on the orfit mask along the central axis of the radiation beam and mark radiation beam outlines on the orfit mask to include shielding needed for organs at risk
- Using 80kV and 12mAs exposure setting on the simulator, take right lateral simulation radiograph for comparison with radiation treatment port films. The simulator film also provides information regarding shielding requirements and thus is a reference for the placement of shielding blocks for organs at risk
- Take patient dimensions and document based on specific bony landmarks to match positions in the treatment plan

Appendix IV: Study protocol on acquisition of Equinox Co-60 unit check films

- Position the patient supine on cobalt-60 treatment unit as per instructions on the patient positioning instruction sheet
- Align the patient in the desired treatment position using alignment lasers fitted within the treatment room with an agreed degree of flexion or extension of the neck
- Use the individualised thermoplastic orfit material to immobilise the head and neck region.
- Align the treatment field along central axis as marked on the orfit immobilisation mask using alignment laser beams
- Using a an exposure setting of 0.01 of a second, take a port film once a week from right lateral side only for the period of treatment of ‘plan 1’ (large volume) for each of the patient in the study
- All port films should be taken at the specified distance of 110cm to match the simulation parameters before radiation treatment is given
- Take one port film once a week on the cobalt -60 radiotherapy unit.
- Process the port films, code as predetermined and keep in respective envelope

Appendix V: Study site Ethics and Research Committee approval letter

Result 3/9/11/2010

RESUBMISSION

Study Site Ethical Committee Letter

Richard Kikwai,
Cape Peninsula University of Technology,
Faculty of Health & Wellness Sciences, GSH Campus,
Radiography E-45 OMB, 7925 Cape Town (South Africa)
29th September 2010.

KENYATTA NATIONAL HOSPITAL RECEIVED 09 MAR 2011 ETHICS & RESEARCH COMMITTEE

The Chairperson,
Ethical Committee
Kenyatta National Hospital,
P.o. Box 20723,
Nairobi, Kenya

Dear Sir/Madam,

Re: Ethical Approval for MTech:Radiography Qualification

I am an employee of KNH working at Cancer treatment centre (CTC) as a senior therapy Radiographer. Currently, I'm enrolled for an MTech: Radiography programme at Cape Peninsula University of Technology (CPUT), Cape Town, South Africa.

I hereby apply for ethics approval to enable me to conduct a research on *'head and neck treatment verification on a cobalt-60 radiation therapy unit'* at CTC. A research proposal is attached for your reference.

KENYATTA NATIONAL HOSPITAL APPROVED 14 APR 2011 ETHICS & RESEARCH COMMITTEE

Ethical requirements will be considered during the entire research period.

Yours sincerely,

Name: Richard Malakwen Kikwai, **P/No.** 530333, **Student No.** 200666843

Sign:..... **Date:** 08/03/2011

Appendix VI: Recommended changes on research proposal by Research Ethics Committee-study site

KENYATTA NATIONAL HOSPITAL,
Hospital Rd. along, Ngong Rd.
P.O. Box 20723, Nairobi.
Tel: 726300-9
Fax. 725272
Telegrams: MEDSUP", Nairobi.
Email: KNHplan@Ken.Healthnet.org

Ref: KNH-ERC/ RR/10

17th January 2011

Richard Malakwen Kikwai
Cape Peninsula University
CAPE TOWN

Dear Richard

Research Proposal: " Head and neck radiation treatment verification on Cobalt-60" (P399/11 /2010)

This is to acknowledge receipt of your research protocol and to inform you that upon review the KNH/UON-Ethics & Research Committee made the following observations and suggestions:

1. Re-organise the protocol to conform to the requirements of the KNH/UON-ERC thus
   - Summary/Abstract
   - Introduction
   - Literature review
   - Research statement, justification, broad objective, specific objectives (numbered) e.t.c.(obtain copy of guidelines from secretariat).
2. Pay attention to the typographical and grammatical errors.
3. Title: Needs to be more clear on Cobalt 60 treatment in order to convey the meaning of the treatment.
4. Provide abstract, even though one is given as a summary in the end, it does not capture the spirit of the document.
5. How was the sample size calculated?
6. Provide a Kiswahili version of the consent information.
7. References must be numbered accordingly.

RECOMMENDATION
Revise and resubmit three (3) copies of the revised proposal within a period of eight (8) weeks with effect from the date of this letter.

Yours faithfully,

PROF A N GUANTAI
SECRETARY, KNH/UON-ERC

c.c. The Deputy Director CS, KNH
Supervisors: Prof. Penelope, Cape Peninsula University of Technology, Cape Town
Dr. Catherine Nyongesa Watta, Cancer Treatment Centre, KNH

Appendix VII: Approval letter to collect data from the Head of Department at study site

The HOD-CTC

P.O BOX 20723,

NAIROBI.

20th April 2011

20/4/2011.
Request approved

Dear Sir,

Re: APPROVAL TO COLLECT DATA

Following approval of the research proposal on 'Head and neck treatment verification on a cobalt-60 radiation therapy unit', I hereby request for clearance from your office on the above subject.

A copy of approval from KNH/UON Ethics and Research Committee is attached for your reference.

Thank you.

Yours Sincerely,

Richard Malakwen Kikwai.

P/No 530333

Student No. 200666843

Appendix VIII: Patient informed consent form in English language

19 APPENDIX E

Participants consent form

Introduction

I am a student at Cape Peninsula University of Technology, South Africa pursuing a Masters programme in Radiography. I am carrying out research on 'head and neck radiation treatment verification on cobalt -60' which involves taking of films once a week on treatment unit during the first four weeks of your treatment. This is to invite you to participate in the study. You will be entered into the study only if you consent to participate after reading, understanding and consenting to the study procedures outlined below by signing in the space provided.

Informed Consent

The radiation treatment is standard treatment and there will be no harm or discomfort associated with this study. Your participation will enable the researchers to learn more about the accuracy of the radiation treatment given on the unit used for your treatment. This study has been reviewed and approved by the applicable Research Ethics Committees of the university and the hospital to ensure that your rights are protected. You may choose either to participate or not and either choice does not affect the quality of treatment you receive. You may choose to withdraw from the study at any time if you decide to. Any information gathered from you will be treated confidentially. Data from this study may go for publication but your identity will not be revealed.

If you have questions or require more information, please contact any of the following:

KENYATTA NATIONAL HOSPITAL APPROVED

Researcher: Richard Kikwai, **Student No.** 200666843, **Tel.** 2726300 Ext.43432, **Cell no.** 0722846062, **E-mail:** kikwairichard @yahoo.com; 200666843@cput.ac.za

Supervisor: Miss Bridget Wyrley-Birch **E-mail:** wyrleybirchb@cput.ac.za

Co supervisor: Prof. Penelope Engel-Hills **E-mail:** engelhillsp@cput.ac.za

External supervisor: Dr. Catherine Nyongesa Watta **Tel.** 2726300 Ext.43484 **Cell no.** 0723698888
E-mail: catherinenyongesa@yahoo.com

If you consent/agree, please sign below,

I consent to participate in the research study on *'head and neck treatment verification on a cobalt -60 radiation therapy unit'* .I have read the information presented in this information letter about a study being conducted by Richard M. Kikwai and have had the opportunity to ask questions about my involvement in this study. With my signature appended here below, I agree to participate in this study.

Signature of participant:..... Date: .....

Participant code number:.....

Appendix IX: Patient informed consent form in Swahili language

19 KIAMBATISHO E

FOMU YA WAFIKI KWA WASHIRIKI

Utanqulizi

Mimi ni mwanafunzi wa shahada ya uzamiti katika fani ya upigaji picha za eksirei(miale-X) katika chuo kikuu cha Kiteknolojia cha **Cape Peninsula, Afrika Kusini.Ninafanya** utafiti unaohusu "uthibitisho wa matibabu ya kichwa **na shingo kwa tiba** redio **kutumia kobalti-60'.Utafiti huu unahusisha** uchukuaji wa filamu mara moja kwa wiki katika kipindi cha wiki nne za kwanza za matibabu yako kwenye kitengo cha matibabu.Huu ni mwaaliko kwako **unaokuomba wewe kushiriki kwenye** utafiti.**Utashirikiswa kwenye** utafiti huu iwapo wewe **mwenyewe utatoa idhini ya kushirikishwa kwako baada ya kusoma,** kuelewa **na** kuridhia utaratibu wa utafiti unaoelezwa hapa chini kwa muhtasari na kasha kutia sahihi katika nafasi iliotolewa.

Wafiki baada ya kuarifiwa

Matibabu kwa tibaredio ni matibabu ya wastani na hakutakuwa na madhara au usumbufu wowote ambao unaweza kuhusishwa na utafiti huu.Kushiriki kwako kutawawezesha watafiti kujua kwa usahihizaidi kiwango cha tibaredio kinachotolewa kwenye kitengo kinachotumika kwa matibabu yako.**Utafiti huu umehakikiwa** na kuthibitishwa na kamati husika za maadili ya utafiti katika chuo kikuu na hospitalini ili kuhakikisha kwamba haki yako inalinwa.Unaweza kuchagua kushiriki au kutoshiriki kwenye utafiti huu.Hata hivyo, kushiriki au kutoshiriki kwako hakuwezi kuathiri ubora wa matibabu unayopokea.Unaweza kujiondoa kwenye utafiti huu wakati wowote iwapo utaamua kufanya hivyo.Habari yoyote itakayo kusanywa kutoka kwako itachukuliwa kama siri.Data kutoka kwenye utafiti huu inaweza kuchapiswa lakini utambulisho wako hautafichuliwa.

Ukiwa na maswali au iwapo unahitaji habari zaidi, unaweza kuwasiliana na yeyote kati ya wafuatao;

Mtafiti : Richard Kikwai (Nambari ya mwanafunzi: 200666843)
Simu : 2726300 *mkondo* 43432. Rununu: 0722846062
Barua pepe : kikwairichard@yahoo.com;200666843@cput.ac.za

Msimamizi : Bi Bridget Wyrley-Birch
Barua pepe : wyrleybircho@cput.ac.za

Msimamizi msaidizi: Prof. Penelope Engel-Hills
Barua pepe : engelhillsp@cput.ac.za

Msimamizi wa nje: **Dkt.Catherine Nyongesa watta**
Simu : 2726300*mkondo* 43484. Rununu :0723698888
Barua pepe : catherinenyongasa@yahoo.com

Iwapo umekubali/unatoa idhini yako,tafadhali tia sahihi hapo chini,
Mimi natoa idhini ya kushiriki katika utafiti unaohusu '*uthibitisho wa matibabu ya kichwa na shingo kwa tibaredio kutumia kobati-60'*.**Nimesoma habari iliyotolewa kwenye makala haya** kuhusu utafiti unaofanywa na Richard M. Kikwai na nimepata fursa ya kuuliza maswali kuhusu kuhusika kwangu katika utafiti huu. Kwa kuiambatisha sahihi yangu hapa chini, ninakubali kushiriki katika utafiti huu.

Sahihi ya mshiriki: ..... Tarehe: .....

Nambari ya siri ya mshiriki: .....
Kikwai, Pendekezo la shahada ya uzamili, chuo kikuu cha Cape Peninsula, (Cape Town).Nambari ya mwanafunzi 200666843

Appendix X: Study approval by the Research Ethics Committee of training institution

Cape Peninsula University of Technology

4 May 2011
CPUT/HW-REC 2011/H09

P.O. Box 1906 • Bellville 7535 South Africa •Tel: +27 21 442 6162 • Fax +27 21 447 2963
Symphony Road Bellville 7535

OFFICE OF THE CHAIRPERSON:
HEALTH AND WELLNESS SCIENCES RESEARCH ETHICS COMMITTEE (HW-REC)
Registration Number NHREC: REC- 230408-014

At the meeting of the Health & Wellness Sciences Research Ethics Committee on 21 February 2011 approval was granted to Richard Malakwen Kikwai pending amendments that have now been received and reviewed. This approval is for research activities related to an MTech: Radiography at this institution.

TITLE:

Head and neck radiation treatment verification on Cobalt-60.

INTERNAL SUPERVISOR: **Ms B Wyrley-Birch**
INTERNAL-CO SUPERVISOR: **Prof P Engel-Hills**

Comment:

Research activities are restricted to those detailed in the proposal and application submitted in November 2010.

Approval will not extend beyond 4 May 2012. An extension must be applied for should data collection for this study continue beyond this date.

Prof PENELOPE ENGEL-HILLS
CHAIR: HEALTH AND WELLNESS SCIENCES RESEARCH ETHICS COMMITTEE

e-mail: *engelhillsp@cput.ac.za*

Appendix XI: Tabulated measured Simulator and Port image values

STUDY PARTICIPANTS	SIMULATION VALUES	PORT FILM VALUES			
		1ST	2ND	3RD	4TH
1.	10	15	15	15	15
2.	30	34	36	36	35
3.	10	14	14	13	14
4.	47	51	51	51	52
5.	62	59	61	63	60
6.	45	41	48	44	48
7.	21	19	24	26	20
8.	58	67	67	66	66
9.	68	66	67	68	68
10.	15	20	17	21	18
11.	39	40	42	41	41
12.	61	62	61	62	63
13.	60	65	66	66	65
14.	27	16	18	18	18
15.	41	40	41	41	41
16.	66	64	63	63	63
17.	16	16	18	20	20
18.	18	16	16	16	16
19.	17	18	17	17	17
20.	45	54	55	54	54
21.	60	59	60	60	59
22.	28	20	19	18	20
23.	21	16	17	16	17
24.	44	53	54	54	54
25.	49	40	40	41	44
26.	15	15	17	19	19
27.	61	66	68	66	65
28.	47	56	57	56	56
29.	39	42	40	41	41
30.	31	30	32	32	33
31.	60	64	64	67	67
32.	25	29	29	28	26
33.					
34.					
35.					

LIST OF REFERENCES

AAPM Report No. 24. See Reinstein, L.E., Amols, H.I., Biggs, P.J., Droege, R.T., Filimonov, A.B., Lutz, W.R. Shalev, S. 1987.

AAPM Task Group 28. See Reinstein, L.E., Amols, H.I., Biggs, P.J., Droege, R.T., Filimonov, A.B., Lutz, W.R. Shalev, S. 1987.

AAPM Task Group 40. See Kutcher, G.J., Coia, L., Gillin, M., Hanson, W., Leibel, S., Morton, R., Palta, J., Purdy, J., Reinstein, L., Svensson, G., Weller, M., & Wingfield, L. 1994.

AAPM Report No. 46. See Kutcher, G.J., Coia, L., Gillin, M., Hanson, W., Leibel, S., Morton, R., Palta, J., Purdy, J., Reinstein, L., Svensson, G., Weller, M., & Wingfield, L. 1994.

AAPM Task Group 53. See Fraass, B., Doppke, K., Hunt, M., Kutcher, G., Starkschall, G., Stern, R., Van Dyke, J. 1998.

AAPM Task Group 58. See Herman, M.G., Balter, J.M., Jaffray, D.A., McGee, K.P., Munro, P., Shalev, S., Van Herk, M., Wong, J.W. 2001.

Al-Sarraf, M., LeBlanc, M., Giri, P.G., Fu, K.K., Cooper, J., Vuong, T., Forastiere, A.A., Adams, G., Sakr, W.A., Schuller, D.E., & Ensley, J.F. 1998. Chemoradiotherapy versus radiotherapy in patients with advanced nasopharyngeal cancer: Phase III randomized intergroup study 0099. *J Clin Oncol*, 16; 1310-1317.

Baker, G.R. 2006. Localisation: Conventional and CT simulation. *Br J Rradiol*, 79;536-549.

Bailet, J. W., Mark, R. J., Abemayor, E., Lee, S.P., Tran, L.M., Juillard, G., Ward, P.H. 1992. Nasopharyngeal carcinoma: treatment results with primary radiation therapy. *Laryngoscope*, 102; 965-72.

Barrett, A., Dobbs, J., Morris, S., Roques, T. 2009. *Practical radiotherapy planning*. Fourth edition. Hodder, Arnold.

Barton, M.B., Frommer, M., & Shafiq, J. 2006. Role of radiotherapy in cancer control in low-income and middle-income countries. *Lancet Oncol*, 7;585-95.

Begnozzi, L., Benassi, M., Bertanelli, M., Bonini, A., Cionini, L., Conte, L., Florino, C., Gabriele, P., Gardani, G., Giani, A., Magri, S., Morelli, M., Morrica, B., Olmi, P., Orecchia, R., Penduzzu, G., Raffaele, L., Rosi, A., Tabocchini, M.A., Valdagni, R., Viti, V. 2009. Quality assurance of 3D-CRT: Indications and difficulties in their applications. *Oncology hematology*, 70 (1); 24-28.

Bel, A., Keus, R., Vijlbrief, R.E., Lebesque, J.V. 1995. Setup deviations in wedged pair irradiation of parotid gland and tonsillar tumours, measured with an electronic portal imaging device. *Radiother Oncol*. 37;153-159.

Bese, N., Munshi, A., Budr ukkar, A., Alzawa, A., Perez, C. 2008. Breast radiation therapy guideline implementation in low and middle-income countries. *American Cancer Society*.

Bissette, R., Boyko, S., Leszczynski, K., Cosby, S., Dunscombe, P., Lightfoot, N. 1995. Radiotherapy portal verification: an observer study. *Br J Radiol*. 68:165-174.

Bogdan, R. C. & Biklen, S. K. 1998. *Qualitative research in education: An introduction to theory and methods (3rd ed).* Needham heights, MA: Allyn & Bacon.

Boyer, A.L., Antonuk, L., Fenster, A., Van Herk, M., Meertens, H., Munro, P., Reinstein, L.E., Wong, J. 1992. A review of electronic portal imaging devices (EPIDs). *Med Phys.* 19:1-16.

Brahme, A. 1984. Dosimetric precision requirements in radiation therapy. *Acta Radiol Oncol,*. 23(5); 379-91.

Brahme, A. 2005. Radiation therapy, *In Physical Methods, Instruments and Measurements*. Encyclopaedia of Life Support Systems (EOLSS), Developed Under The Auspices of the UNESCO, Eolss Publishers, Oxford, UK, [http://www.eolss.net]

Brink, H. Van de Walt, C. & van Rensburg, 2nd ed. 2006. *Fundamentals of Research Methodology for Health care Professionals.* Cape Town, Landsdowne.

Brink, H. I. 2000. *Fundamentals of research methodology for health care professionals*. Juta & Company Ltd.

Burns, N. & Grove, S.K. 2003. *Understanding nursing Research*. (3rd ed.). Saunders, Elsevier.

Canadian Association of Provincial Cancer Agency (CAPCA). 2007. See Dunscombe, P., Johnson, H., Arsenault, C., mawko, G., Bissonnette, J.P., Seuntjens, J. 2007.

Caglar, H.B., Allen, A.M. 2007. Intensity-Modulated radiotherapy for head and neck cancer. *Clinical Advances in Haematology & Oncology*. Vol. 5; 6.

Chan, A.T.C., Teo, P.M.L., & Johnson, P.J. 2002. Nasopharyngeal carcinoma. *Annals of Oncology* 13; 1007-1015.

Chan, A.T.C., Teo, P.M.L., Leung T.W.T, & Johnson, P.J. 1998. The role of chemotherapy in the management of nasopharyngeal carcinoma. *American Cancer Society*, 82; 1003-12.

Chang, E.T., Adami, H.O. 2006. The enigmatic epidemiology of nasopharyngeal carcinoma. *Cancer Epidemiol Biomarkers Prev*, 15;1765-1777.

Charles, C.M. 1995. Introduction to educational research (2nd ed.) San Diego, Longman.

Chatani, M., Matayoshi, Y., Masaki, N., Fujii, T., Umatani, K., Yoshino, K. 1993. Radiation therapy of the nasopharyngeal carcinoma: treatment results and prognostic factors. *Strahlenther Onkol*, 169;527-33.

Cheng, S.H., Yen, K.L., Jian, J.J., Tsai, S.Y., Chu, N.M., Leu, S.Y., Chan, K.Y., Tan, T.D., Cheng, J.C., Hsieh, C.Y., Huang, A.T. 2001. Examining prognostic factors and patterns of failure in nasopharyngeal carcinoma following concomitant radiotherapy and chemotherapy: Impact on future clinical trials. *Int J Radiat Oncol Biol Phys*, 50; 717-726.

Ching, F.K. 2009. Modern advances in Radiotherapy. *Malaysian Oncology Society*.

Chow, E., Payne, D., O'Sullivan, B., Pintilie, M., Liu, F.F., Waldron, J., Warde, P., & Cummings, B. 2002. Radiotherapy alone in patients with advanced nasopharyngeal cancer: Comparison with an intergroup study. Is combined modality treatment really necessary? *Radiother Oncol*, 63;269-274.

Chua, D.T., Sham, J.S., Wei, W.I., Ho, W.K., & Au, G.K. 2001. The predictive value of the 1997 American Joint Committee on Cancer stage classification in determining failure patterns in nasopharyngeal carcinoma. *Cancer*, 92; 2845-2855.

Clifford, P. 1972. Carcinoma in the nose and throat: Nasopharyngeal carcinoma in Kenya. *Proc Roy Soc Med*, 65.

Cottrill, C.P., & Nutting, C.M. 2003. Tumours of the nasopharynx. In Rhys Evans, P.H., Montgomery, P.Q., & Gullane, P.J. *Principles and practice of head and neck oncology*. Taylor & Francis group.

Curado, M.P,. Edwards, B.K,. Shin, H.R,. Storm, H,. Ferlay, J., Haenue, M., & Boyle, P. 2007. Cancer incidence in five continents. Vol. IX. *IARC Scientific Pub*, 160. Lyon, France.

Denscombe, M. 2002. *Ground rules for good research: a 10 point guide for social researchers.* Philadelphia: Open University.

Department of medical records. 2010. Impact of cancer disease at KNH 1998-2008. Medical records, statistics unit, Kenyatta National Hospital, Nairobi, Kenya.

Dobbs, J., Barrett, A., & Ash, D; 3rd Ed; 1999. *Practical radiotherapy planning*. Arnold, Bristol.

Droege, R.T. & Bjarngard, B.E. 1979a. Influence of metal screens on contrast in megavoltage x-ray imaging. *Med Phys*, 6;487-93.

Droege, R.T. & Bjarngard, B.E. 1979b. Metal screen-film detector MTF at megavoltage x-ray energies. *Med Phys*, 6; 487-93.

Droege, R.T. & Stefanakos, T.K. 1985. Portal film technique charts. *Int J Rad Oncol Biol Phys*, 11; 2027-2032.

Dunscombe, P., Johnson, H., Arsenault, C., Bissonnette, J-P., Johnson, H., Mawko, G., & Seuntjens, J .2007. Development of quality control standards for radiation therapy equipment in Canada. *Journal of Applied Clinical Medical Physics*, Vol.8,1;108-118.

Faithfull, S. & Wells, M. 2003. *Supportive care in Radiotherapy.* Edinburgh: Churchill Livingstone.

Ferlay, J., Shin, H.R., Bray, F., Forman, D., Mathers, C., Parkin, D.M. 2011. Estimates of worldwide burden of cancer in 2008. GLOBOCAN 2008. *Int J Cancer*, 15; 127 (12) 2893-917.

Fogarty, G.B., Hornby, C., Ferguson, H.M., & Peters, L.J. 2001. Quality assurance in radiation oncology unit: The chart round experience. *Australasian Radiology*, 45;189-194.

Fraass, B., Doppke, K., Hunt, M., Kutcher, G., Starkschall, G., Stern, R., Van Dyke, J. 1998. American Association of Physicists in Medicine (AAPM). Radiation Therapy Task Group 53: Quality assurance for clinical radiotherapy treatment planning. *J Med. Phys*, 25(10).

Gildersleve, J., Dearnaley, D.P., Evans, P.M., Swindell, W. 1995. Reproducibility of patient positioning during routine radiotherapy, as assessed by an integrated megavoltage imaging system. *Radiother Oncol*, 35;151-160.

Golafshani, N. 2003. *Understanding reliability and validity in qualitative research*. Toronto, Canada:University of Toronto,

Goitein, M., Abrams, M., Rowell, D., Pollari, H., & Wiles, J. 1983. Multidimentional treatment planning 11 beam's eye view, back projection and projection through CT section. *Int J Rad Oncol Biol Phys*, 9; 789-797.

Goitein, M. & Busse, J. 1975. Immobilisation error: some theoretical considerations. *Radiology*, 117; 406-12.

GraphPad PRISM. 1992-2012. Prism 6 for windows version (Trial). GraphPad Software, Inc.

Hammoudah, M.M. & Henschke, K. 1977. Supervoltage x-ray beam films. *Int J Radiat Oncol Biol Phys*, 2; 571-7.

Haus, A.G. *Film systems for radiotherapy imaging*. In Hale, J.D., Boyer, A.L. 1998. Imaging in radiation therapy, AAPM Medical Physics monograph No.24. *Medical Physics Publishing*. 179-206.

Her, C. 2001. Nasopharyngeal cancer and the Southeast Asian patient. *American family Physician*, 63;1776-82,1785.

Herman, M.G., Kruse, J.J., Hagness, C.R. 2000. Guide to clinical use of electronic portal imaging. *J of Applied Clinical Medical Phys*, 1; 2.

Herman, M.G., Balter, J.M., Jaffray, D.A., McGee, K.P., Munro, P., Shalev, S., Van Herk, M., Wong, J.W. 2001. Clinical use of electronic portal imaging: report of AAPM Radiation Therapy Task Group 58. *American Association of Physicists in medicine*.

Hess, C.F., Kortmann, R.D., Jany, R., Hamberger, A., Bamberg, M. 1995. Accuracy of field alignment in radiotherapy of head and neck cancer utilizing individualized face mask immobilization: a retrospective analysis of clinical practice. *Radiother Oncol*, 33;157-166.

Hicks, C.M. 2004. *Research methods for clinical therapists. Applied project design and analysis.* Churchill Livingstone, Elsevier Science.

Hildesheim, A., & Levin, P.H. 1993. Etiology of nasopharyngeal carcinoma. A review. *Epidermiol Rev*, 15; 466-485.

Ho, J.H.C. 1978. An epidemiologic and clinical study of nasopharyngeal carcinoma. *Int J Rad Oncol Biol Phys*. 4; 183-205

Hsu, W., Chen, S., Ying, K., Jand, C., Wang, P., Lin, G. 2003. A comparison of treatment plans for recurrent nasopharyngeal carcinoma. *Chi J Radiol*, 28;285-292.

Huizenga, H., Levendag, P.C., De Porre, P.M., & Visser, A.G. 1988. Accuracy in radiation field alignment in head and neck cancer: a prospective study. *Radiother Oncol*, 11; 181-187.

Hulley, S. B., Cummings, S.R., Browner, W.S., Grady, D.G. & Newman, T.B. 2007. *Designing Clinical Research*. Philadelphia: Lippincott Williams & Wilkins.

Hunt, M.A., Kutcher, C., Burman, D. Fass, L., Harrison, S, Leibel, & Z, Fuks. 1993. The Effects of Treatment uncertainties on the treatment of Nasopharynx Cancer. *Int.J.Radiation.Oncol.Biol.Phys.* 27; 437-447.

Hunt, M.A., Schultheiss,.T.E., Desobry, G.E., Hakki,M., & Hanks, G.E. 1995. An evaluation of setup uncertainities for patients treatet to pelvic sites. *Int.J.Radiation.Oncol.Biol.Phys*, 32; 227-33.

Hurkmans, C. W., Remeijer. P., Lebesque, J.V., & Mijnheer, B.J. 2001. Set-up verification using portal imaging; review of current clinical practice. *Radiotherapy and oncology, 58:*105-120. www.elsevier.com/locate/radonline [Accessed 4th October 2010].

International Atomic Energy Agency (IAEA). 2008. *Setting up a Radiotherapy programme: Clinical, Medical physics, Radiation protection and safety aspects*. Vienna: International Atomic Energy Agency.

International Atomic Energy Agency (IAEA). 2005. *Radiation Oncology Physics: A Handbook for teachers and students.* Vienna: International Atomic Energy Agency.

International Atomic Energy Agency (IAEA). 2003. *A silent crisis. Cancer treatment in developing countries.* Vienna: International Atomic Energy Agency.

International Atomic Energy Agency (IAEA). 1996. *Safety Series No. 115. International basic safety standards for protection against ionizing radiation and for the safety of radiation sources.* Vienna: International Atomic Energy Agency..

International Commission on Radiation Units and Measurements (ICRU). 1999. *ICRU Report 62: Prescribing, recording, and reporting photon beam therapy. (Supplement to ICRU Report, 50).* Bethesda, MD: ICRU Publications.

International Commission on Radiation Units and Measurements (ICRU). 1993. *Prescribing, recording, and reporting photon beam therapy, ICRU Report, 50.* Bethesda, MD: ICRU Publications.

International Commission on Radiation Units and Measurements (ICRU). 1976. *Determination of dose in a patient irradiated by beams of X or Gamma rays in radiotherapy procedures, ICRU report 24*. Bethesda, MD: ICRU Publications.

Jackson, C. 1901. Primary carcinoma of the nasopharynx: a table of cases. *JAMA*, 31; 371-7.

Jaffray, D.A., & Dawson, L.A. 2007. Advances in image-guided radiation therapy. *J of clinical Oncol*, 25(8); 938-946.

Jeannel, D., Hubert, A.. & DeVathaire, F. 1990. Diet living conditions and NPC in Tunisia. *Int J Cancer*, 46; 421-425.

Jemal, A., Bray, F., Center, M.M., & Ferlay, J. 2011. Global cancer statistics. *CA Cancer J Clin*, 61;69-90.

Johansen, L.V., Mestre, M., & Overgaard, J. 1992. Carcinoma of the nasopharynx: analysis of treatment results in 167 consecutively admitted patients. *Head and neck*, 14;200-7.

Khan, F.M. & Potish, R.A. 1998. *Treatment planning in Radiation Oncology*. Baltimore: Williams & Wilkins.

Klein, G. 2002. Nasopharyngeal carcinoma (NPC) is an enigmatic tumour. *Semin Cancer Biol*, 12;415-418.

Kristensen, C.A. 2007. Functional preservation and quality of life in head and neck radiotherapy. Paranasal sinuses and nasal cavity. *Medical Radiobiology*, 1;75-87.

Kutcher, G.J., Coia, L., Gillin, M., Hanson, W., Leibel, S., Morton, R., Palta, J., Purdy, J., Reinstein, L., Svensson, G., Weller, M., & Wingfield, L. 1994. Comprehensive QA for radiation oncology: report of AAPM Radiation Therapy Committee Task Group 40. *Med. Phys.* 21:581-618.

Kwong, D.L.W., Sham, J.S.T., Au, G.K.H., Chua, D.T.T., Kwong, P.W.K., Cheng, A.C.K., Wu, P.M., Law, M.W.M., Kwok, C.C.H., Yua, C.C., Wan, K.Y., Chan, R.T.T., & Choy, D.D.K. 2004. Concurrent and adjuvant chemotherapy for nasopharyngeal carcinoma: A factorial study. *J Clin Oncol*, 21; 631-637.

Langmack, K.A. & Goss, V. 1999. Characterization of new portal film systems for radiotherapy verification. *Br J Radiol*, 72:479-84.

Langmack, K.A. 2001. Portal imaging. *Br J Radiol*, 74; 789-804.

Lee, P.C. & Glasgow, G.P. 1998. Technique charts for Kodak's new film-screen systems for portal localization. *Med Dosim*, 23;113-6.

Lee, N., Xia, P., Quivey, J. M., Sultanem, K., Poon, I., Akazawa, C., Akazawa, P., Weinberg, V., & Fu, K.K. 2002. Intensity-modulated radiotherapy in the treatment of nasopharyngeal carcinoma: an update of the UCSF experience *Int J Rad Oncol Biol Phy*, 53;12-22

Lee, A., Poon, Y., Foo, W., Law, S., Cheung, F., Chan, D., Tung, S., Thaw, M., & Ho, J.H.C. 1992. Retrospective analysis of 5037 patients with nasopharyngeal carcinoma treated during 1976-1985: Overall survival and pattern of failure. *Int J Radiat Oncol Biol Phys*, 23;261-70.

Leedy, P.D. & Ormrod, J.E. 2005. *Practical research- planning and design*. New Jersey: Pearson Merrill Prentice Hall.

Leedy, P.D. & Ormrod, J.E. 2010. *Practical research- planning and design.* New Jersey: Pearson Merrill Prentice Hall.

Levin, C.V., El Gueddari, B. & Meghzifene, A. 1999. Radiation therapy in Africa: distribution and Equipment. *Radiotherapy and oncology J. (*52) ,79-84.

Lin, J.C., Jan, J.S., Hsu, C.Y. 2003. Phase III study of concurrent chemoradiotherapy versus radiotherapy alone for advanced nasopharyngeal carcinoma: Positive effect on overall and progressive-free survival. *J Clin Oncol*, 21;631-637.

Lin, J., Wang, W., Chen, K., Wei, Y., Liang, W., Jan, J., & Jiang, R. 2004. Quantification of plasma Epstein-Barr virus DNA in patients with advanced nasopharyngeal carcinoma. *N Engl J Med*, 350; 2461-2470.

Lirette, A., Pouliot, J., Aubin, M., & Larochelle, M. 1995. The role of electronic portal imaging in tangential breast irradiation: A prospective study. *Radiother Oncol*, 37; 241-245

Lo, Y., Chan, L., Chan, A., Leung, S., Lo, K., Zhang, J., Lee, J., Hjelm, N., Johnson, P., & Huang, D. 1999a. Quantitative analysis of cell-free Epstein-Barr virus DNA in plasma of patients with nasopharyngeal carcinoma. *Cancer Res*, 59; 1188-1191.

Lo, Y., Chan, L., Chan, A., Leung, S., Lo, K., Zhang, J., Lee, J., Hjelm, N., Johnson, P., & Huang, D. 1999b. Quantitative and temporal correlation between circulating cell-free Epstein-Barr virus DNA and tumour recurrence in nasopharyngeal carcinoma. *Cancer Res*, 59;5452-5455.

Lo, Y.M., Leung, S., Chan, L., Chan, A., Lo, K., Johnson, P., & Huang, D. 2000. Kinetics of plasma Epstein-Barr virus DNA during radiation therapy for nasopharyngeal carcinoma. *Cancer Res*, 60; 2351-2355.

Marks, J.E., Haus, A.G., Sutton, H.G, & Griem, M.L. 1976. The value of frequent treatment verification film in reducing localisation errors in the radiation of complex fields. *Cancer* 37; 2755-61.

Maree, K. (ed.) 2007. *First steps in research.* Pretoria: Van Schaik.

Mason, J. 2002. *Qualitative researching.* 2nd edition. London: Sage.

McCarty, P.J. & Million, R.R. History of diagnosis and treatment of cancer of the head and neck. In: Million, R.R. & Cassisi, N.J. 1994. *Management of head and neck cancer a multidisciplinary approach.* Philadelphia, JB Lippincott.

McJury, M., Dyker, K., Nakielny, R., Conway, J., & Robinson, M.H. 2006. Optimizing localization accuracy in head and neck, and brain radiotherapy. *The British J of Radiology*, 79;672-680.

Meertens, H., van Herk, M., Bijhold, J., & Bartelink, H. 1990. First clinical experience with a newly developed electronic portal imaging device. *Int J Radiat Oncol Biol Phys*, 18; 1173-81.

Milecki, P., Nowrocki, S., Malicki, J., & Stryczynska, G. 2001. Evaluation of an electronic portal imaging device (Target view, GE) as a quality assurance tool. *Rep Pract Onco Radiother,* 4(4).

Mileusnic, D. 2005. Verification and correction of geometrical uncertainties in conformal radiotherapy. *Achive of Oncology*, 13; 3-4, 140-144.

Mitine, C., Dutreix, A., Van der Schueren, E. 1993. Black and white in accuracy assessment of megavoltage images: the medical decision is often grey. *Radiother Oncology*, 28; 31-36.

Mould, R. F., & Tai T.H.P. 2002. Nasopharyngeal carcinoma: treatment and outcomes in the 20th century. Br J Radiol. 75; 307-339.

Mouton, J. 2001. *Understanding social research*. Pretoria: J.L. Van Schuik Academic.

Naiyanet, N., Oonsiri, S., Lertbutsayanukul, C. & Suriyapee, S. 2007. Measurements of Patients setup variation in intensity-modulated Radiation Therapy of Head and Neck cancer using electronic portal imaging device. *Biomed Imaging Inter*. J. 3(1);e30 http://www.biij.org/2007/1/e30 [Accessed 20th August 2010].

National Cancer Control Strategy (NCCS). 2011-2016. Ministry of Public Health and Sanitation and Ministry of Medical Services. Republic of Kenya.

NC State University. 2004. Lab Write resources. www.ncsu/labwrite September 2012.

New, G.B., & Stevenson, W. 1943. End results of malignant lesions of the nasopharynx. *AMA Arch Otolaryngolo*, 38; 205-9.

Nicolaou, N. 1999. Radiation therapy treatment planning and delivery. *Seminars in Oncology Nursing, Vol. 15 (4), 260-269.*

Parker, W., & Patrocinio, H. Clinical treatment planning in external photon beam radiotherapy. In Podgorsak, I. 2005. *Radiation Oncology Physics: A Handbook for Teachers and Students.* Vienna: International Atomic Energy Agency (IAEA).

Parkin, D.M., Whelan, S., Ferlay, J., Bah, E., & Hamdi-Cherif, M. 2003. Cancer in Africa. *IARC Pub, 153*. Lyon France.

Parkin, D., Bray, F., Ferlay, J., & Pisani P. 2005. Global cancer statistics 2002. Predicting the future burden of cancer. *CA cancer J Clin*, 55;74-108

Parsons, C.L. 1999. Obtaining ethical approval for health sciences research. In Minichiello, V., Sullivan, G., Greenwood, K., & Axford, R. *Handbook for research methods in health health sciences.* Addison-Wesley.

Pehlivan, B., Pichenot, C., Castaing, M., Auperin, A., Lefkopoulos, D., Arriagada, R., Bourhis, J. 2009. Interfractional set-up errors evaluated by daily electronic portal imaging of IMRT in head and neck cancer patients. *Acta Oncologica*, 48;440-445.

Peiffert, D., Simon, J.M., and Eschwege, F. 2007. Epinal radiotherapy accident: passed, present, future. *Cancer Radiother*, 11(6-7); 309-12.

Perera, T., Moseley, J. & Munro, P. 1999. Sudjectivity in interpretation of portal films. *Int J Radiat Oncol Biol Phys*, 45;529-534.

Podgorsak, I. 2005. *Radiation Oncology Physics: A Handbook for Teachers and Students.* Vienna: International Atomic Energy Agency (IAEA).

Polit, D.F., Beck, C.T. and Hungler, B.P. 2001. *Essentials of Nursing Research: Methods, Appraisal and Utilization*. 5th Ed., Philadelphia: Lippincott Williams & Wilkins.

Parkin, D.M., Bray, F., Ferlay, J., & Pisani, P. 2005. Global cancer statistics, 2002. *CA Cancer J Clinicians*, 55; 74-108.

Ravichandran, R. 2009. Has Time come for doing away with Cobalt-60 teletherapy for cancer treatments. *J.Med Phy. Apr-Jun,* 34(2); 63-65.

Razak, A.R.A., Sui, L. L., Liu, F., Ito, E., O'Sullivan, B., & Chan, K. 2010. Nasopharyngeal carcinoma: The next challenges. *European Journal of cancer*, 46;1967-1978.

Reinstein, L.E., Amols, H.I., Biggs, P.J., Droege, R.T., Filimonov, A.B., Lutz, W.R. Shalev, S. 1987. American Institute of Physics. The Association of Physicists in medicine.

Roberts, R. 1996. Portal imaging with film-cassette combinations: what film should we use? *Br J Radiol*, 69; 70-1.

Rogues, T., Dagless, M., & Tomes, J. 2005. Randomised trial on two types of thermoplastic masks for patient immobilization during radiation therapy for head and neck cancer. *Inter J Radiat Oncol Biol Phys*, 62(3);942.

Rovirosa, A., Berenguer, J., Sanchez-Reyes, A., Farrus, B., Casas, F., & Biete, A. 1995. CT-Based Simulation For head and neck tumours in centres without CT-Simulator and 3D-planning System. *Medical Dosimetry. Vol*. 20 (2); 111-115.

Royal College of Radiologists (RCR), 2008. *On target: Ensuring geometric accuracy in radiotherapy*. London, the Royal College of Radiologists.

Salminen, E., Izewska, J., & Andreo, P. 2005. IAEA's role in the global management of cancer-focus on upgrading radiotherapy services. *Octa Oncologica*, 44; 816-824.

SASSA – South African Social Security Agency. 2008. *Glossary of key terms in monitoring and evaluation: Tools Series 2.* http://www.cop-mfdr_africa.org/forum/attachment/download [29 July 2012].

Sham, J.S, Choy, D., Choy, P.H. 1990. Nasopharyngeal carcinoma: The significance of neck node involvement in relation to the pattern of distant failure. *Br J Radiol*, 63; 108-113.

Sharp, L., Lewin, F., Johansson, H., Payne, D., Gerhardsson, A., & Rutqvist, L. 2005. Randomised trial on two types of thermoplastic masks for patient immobilization during radiation therapy for head and neck cancer. *Inter J Radiat Oncol Biol Phys*, 61(1);250-256.

Sica, G.T. 2006. Bias in research studies. *Radiology*, 238; 780-789.

Sikora, K. 1999. Developing a global strategy for cancer. *Eur Journal of cancer, Vol.35 (1); 24-31*. Elsevier Science Ltd. Great Britain.

Spano, J.P., Busson, P., Atlan, D. Bourhis, J., Pignon, J.P., Esteban, C., & Armand. 2003. Nasopharyngeal carcinoma: an update. *Eur Journal of cancer, Vol.39;2121-2135.* Pergamon, Elsevier Ltd.

Stroom, J.C. & Heijmen, B.J.M. 2002. Geometric uncertainties, radiotherapy planning margins, and the ICRU-62 report. *Radiotherapy and oncology*, 64; 75-83.

Suter, B., Shoulders, B. Maclean, J. 2000. Machine verification radiographs: an opportunity for role extension? *Radiography* 6, 245-251.

Swinburne, K. 1971. Pattern recognition for radiographers. *Lancet*, 589-90.

Thwaites, D.I., Mijnheer, B.J., Mills, J.A. 2005. Quality assurance of external beam radiotherapy in Podgorsak, E.B. 2005. *Radiation Oncology Physics: A Handbook for Teachers and Students.* Vienna: IAEA.

Thwaites, D., Scalliet, P. Leer, J.W., Overgaard, J. 1995. Quality assurance in radiotherapy. European Society for Therapeutic Radiology and Oncology Advisory Report to the Commission of the European Union for the 'Europe Against Cancer Programme'. *Radiother Oncol*, 35(1); 61-73.

Thompson, L.D.R. 2007. Update on nasopharyngeal carcinoma. *Head and Neck Pathol*, 1;81-86.

Tong, A. C., Leung, A. C., Sham, J. 1999. Incidence of complicated healing and osteoradionecrosis following tooth extraction in patients receiving radiotherapy for treatment of nasopharyngeal carcinoma. *Australian Dental Journal*, 44(3); 187-194.

Torgil, M. 1996. Head and neck cancer. *Octa Oncologica*, 35;22-45.

Tsai, J.S., Engler, M.J., Ling, M.N., Wu, J.K., Kramer, B., Dipetrillo, T., & Wazer, D.E. 1999. A non-invasive immobilization system and related quality assurance for dynamic intensity modulated radiation therapy of intracranial and head and neck disease. *Int J Radiat Oncol Biol Phys*, 43;455-467.

UICC, 1997. *5th International Union Against Cancer (UICC) Classification. TNM classification of malignant tumours.* 5th edn. Germany, springer Verlag.

Van Dyk, J. 1999. *The Modern Technology of Radiation Oncology* 1st ed. Madison Wisconsin: Medical Physics Publishing.

Van Elmpt, W., McDermott, L., Nijsten, S., Wendling, M., Lambin, P., & Mijneer, B. 2008. A literature review of electronic portal imaging for radiotherapy dosimetry. *Radiot and Oncol*, 88;289-309.

Van de Geijn, J., Harrington, F.S., Fraass, B.A. 1982. A graticule for evaluation of megavoltage x-ray port films. Int. J Rad Oncol Biol Physics, (8),11; 1999-2000.

Van Lin, E., Van der Vight, L., Huizenga, H., Kaanders, J., & Visser, A. 2003. Set-up improvement in head and neck radiotherapy using 3D off-line EPID based correction protocol and a customized head and neck support. *Radiother and Oncol*, 68; 137-148.

Van Teijlingen, E.R., & Hundley, V. 2001. The importance of pilot studies. Issue 35. *Social research update*. University of Surrey, Guildford GU7 5XH, England

Visser, A.G., Huizenger, H., Althof, V.G., & Swanenburg, B.N. 1990. Performance of a prototype fluoroscopic radiotherapy imaging system. *Int J Radiat Oncol Biol Phys*, 18; 43-50.

Vokes, E.E., Liebowitz, D.N., & Weichselbaum, R.R. 1997. Nasopharyngeal carcinoma. *The Lancet*. 250; 1087-91.

Vos, P., Van Riel, V., De Winter, K. 1997. 3D measurements and correlation of systematic patient setup errors in external irradiation of patients with a brain tumour, using digital portal imaging. In: Leavitt, D.D., & Starkschall, G. Proceedings of the XIIth international congress of computers in radiotherapy, Madison, WI: *Medical Physics Publishing*. 223-226.

Wanja, J. 2010. *Kenya's new silent killer*. Daily nation newspaper, Wednesday 19 /09/2010 http://www.nation.co.ke/magazines/Kenyas%20silent%20killer%20/-/1190/1013946/-/6tq5kv/-/index.html [Accessed 20th September 2010]

Waldron, J., Tin, M.M., Keller, A., Lum, C., Japp, B., Sellmann, S., Van Prooijen, M., Gitterman, L., Blend, R., Pyne, D., Liu, F.F., Warde, P., Cummings, B., Pintilie, M., & O'Sullivan, B. 2003. Limitations of conventional two dimentional radiation therapy planning in nasopharyngeal carcinoma. *Radiotherapy and Oncology* 68; 153-161

Wei, I.W. & Sham, J.S.T. 2005. Nasopharyngeal carcinoma. *Lancet*, 365;2040-54.

Wells, W. 1998. The hidden experience of radiotherapy to the head and neck: a qualitative study of patients after completion of treatment. *Journal of advanced nursing*, 28 (4); 840-848.

Weltens, O., Kesteloot, K., Vandevelde, C., Van den Bogaert, W. 1995. Comparison of plastic and orfit masks for patient head fixation during radiotherapy: precision and cost. *Int J Radiat Oncol Biol Phys*, 33; 499-507.

Willner, J., Hadinger, U., Neumann, M., Schwab, F.J., Bratengeier, K., & Flentje, M. 1997. Three dimensional variability in patient positioning using bite block immobilisation in 3D-conformal radiation treatment for ENT tumours. *Radiother Oncol*, 43; 315-321.

World Health Organization (WHO). 2010. Kenya country office, in Medical records, 2010. Statistics unit. Impact of the cancer disease at KNH, *1998-2008*. Institutional document.

World Health Organization (WHO). 2008a. *Policy and Advocacy. Cancer Control. Knowledge into action. WHO Guide for effective Programmes.* Geneva.: World Health Organization.

World Health Organization (WHO). 2008b. *World cancer report*. Geneva: International Agency for Research on Cancer.

World Health Organization (WHO). 2003. *Cancer in Africa. Epidemiology and prevention*. Lyon: IARC Press, Lyon.

World Health Organization (WHO). 2002. National Cancer Control Programmes. Policies and managerial Guidelines. World Health Organization, Geneva.

World Health Organization (WHO). 1995. *Treatment of cancer. Policies and managerial Guidelines.* Geneva: World Health Organization..

World Health Organization (WHO). 1988. *Quality assurance in radiotherapy*. Geneva: World Health Organization.

World Health Organization (WHO). 1978. *Histological typing of upper respiratory tract tumours. International histological classification of tumours*. Geneva: World Health Organisation.

Xu, L., Pan, J., Wu, J., Pan, C., Zhang, Y., Lin, S., Yang, L., Chen, C., Zhang, C., Zheng, W., Lin, S., Ni, X., & Kong, F. 2010. Factors associated with overall survival in 1706 patients with nasopharyngeal carcinoma: significance of intensive neoadjuvant chemotherapy and radiation break. *Radiother and Oncol*, 96; 94-99.

Yan, D., Wong, J., Vicini, F., et al. 1997. Adoptive modification of treatment planning to minimize the deleterious effects of treatment setup errors. *Int J Radiat Oncol Biol Phys*, 38; 197-206.

Yan, J., Qin, D., Hu, Y., Cai, W., Xu, G., Wu, X, Li, S., & Gu, X. 1988. Management of local residual primary lesion of nasopharynx carcinoma (NPC), Part 1: Are higher doses beneficial? *Int J Radiat Oncol Biol Phys*, 2; 1- 5.

Yan, J., Qin, D., Hu, Y., Cai, W., Xu, G., Wu, X, Li, S., & Gu, X. 1989. Management of local residual primary lesion of nasopharynx carcinoma: are higher doses beneficial? *Int J Radiat Oncol Biol Phys*,16; 1465-9.

Yan, J., Xu, G., Hu, Y., Li, S., Lie, Y., Qin, D., Wu, X., & Gu, X. 1990. Management of local residual primary lesion of nasopharynx carcinoma:II. Results of prospective randomised trial on booster dose. *Int J Radiat Oncol Biol Phys*, 18; 295-8.

Yi, J., Gao, L., Huang, X., Li, S., Luo, J., Cai, W., Xiao, J., & Xu, G. 2006. Nasopharyngeal carcinoma treated by radical radiotherapy alone: ten year experience of a single institution. Int J Radiation *Oncol Biol Phys*, 65; (1) 161-168.

Yu, M.C. 2006. Nasopharyngeal cancer. In: Schottenfeld, D. & Freumeni, J.F. 2006. *Cancer epidemiology and prevention*. New York. Oxford University press.