SKIN CANCER IN NIGERIA AND OUTCOME TREATMENT IN PATIENTS SEEN AT THE RADIOTHERAPY DEPARTMENT, UNIVERSITY COLLEGE HOSPITAL, IBADAN.


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NOVEMBER 2013
DECLARATION

I declare that this study has not been previously submitted to any other college for consideration or elsewhere for publication

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DR. OKWOR VITALIS CHUKWUEMEKA DATE
CERTIFICATION

This is to certify that this project titled; **SKIN CANCER IN NIGERIA AND OUTCOME OF TREATMENT IN PATIENTS SEEN AT THE RADIOTHERAPY DEPARTMENT OF UNIVERSITY COLLEGE HOSPITAL (UCH), IBADAN** was carried out by **DR OKWOR VITALIS CHUKWUEMEKA** of the department of Radiotherapy university college hospital, Ibadan, under my supervision

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This book is dedicated to God Almighty for his grace and favour, my teachers and colleague, the patients through whom I gained experience, and my family for their love and support.
ACKNOWLEDGEMENT

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# TABLE OF CONTENTS

Title Page..............................................................................................................................................i
Declaration...............................................................................................................................................ii
Attestation...............................................................................................................................................iii
Table of Contents........................................................................................................................................iv
Abstract......................................................................................................................................................1
Introduction..............................................................................................................................................3
Justification.............................................................................................................................................5
Aims And Objectives...............................................................................................................................6
Literature Review.....................................................................................................................................7
Materials and Methods.........................................................................................................................38
Result.......................................................................................................................................................40
Discussion..............................................................................................................................................55
Conclusion..............................................................................................................................................60
Recommendation.....................................................................................................................................61
References...............................................................................................................................................62
Appendix 1 WHO Classification of Skin cancer....................................................................................73
Appendix 2 AJCC TNM Staging Classification of Skin Cancer.................................................................74
Appendix 3 Data Extraction Form .........................................................................................................75
ABSTRACT

Skin cancer is the commonest neoplastic condition presenting to the physician in the Caucasian population. It is conveniently classified into non-melanoma skin cancers (NMSC) and melanoma. Melanoma is the most severe form of skin cancer, it comprises only 3% of all skin cancers and accounts for about 75% of skin cancer mortality. The non-melanoma group encompasses all other skin cancers and has a clinical course ranging from indolent to very aggressive form depending on the histology. Basal cell carcinoma is the commonest non-melanoma skin cancer and constitute about 80% worldwide. Skin cancer is the sixth top ten cancers in Nigeria. It is most common in the seventh and eighth decades of life with slight male predominance. They are rare in dark-skinned races. Skin cancers metastasise through the lymphatics to the regional lymph nodes and haematogously to the viscera commonly to the lungs, liver, brain and bones. At early presentation, basal and squamous cell carcinomas can be cured in over 90% of cases by variety of techniques while in late presentation the treatment is palliative.

It is thus the aim of this study to evaluate the outcome of skin cancer treatment in patients seen and being managed in the Radiotherapy Department of the UCH Ibadan.

The data extraction form was used to obtain information from the Radiotherapy treatments records and the case notes of patients with histological diagnosis of skin cancers between January 2001 and December 2010 at the Radiotherapy department, University College Hospital, Ibadan.

Data collected was be analyzed using the Statistical package for social sciences (SPSS) Version 16.0

The age of patients ranged from 7 to 98 years with mean age of 46.6 years. The male to female ratio was 1.5. The peak age of incidence was between 40-49 years. Most patients presented with stage III and IV. Lower limb and gluteal region had the highest proportion of occurrence 75(59.9%), followed by the head and neck. Lung had the commonest site of distant metastasis followed by liver. A higher proportion 41(96%) of patients that presented at early stage had excision surgery. 78(63.9%) of patients received radiotherapy with dose range of 40-49Gy. A higher number of patients 54(54.5%) had chemotherapy mostly Cisplatin and 5
fluorouracil. A higher proportion 9(50%) for stage I and 12(44.4%) for stage II disease of patient had more symptoms free interval.

Squamous cell carcinoma was the commonest histology sub-type in this study and trauma was found to be the commonest cause of skin cancer in this environment. Lower limb was the predominant site of skin cancer involvement while lung was the commonest site of metastases. Early stage disease had higher proportion of patients with one and two years symptom free interval. More efforts should be made toward early detection and treatment.
INTRODUCTION;

Skin cancer is the commonest neoplastic condition presenting to the physician in the Caucasian population.\(^1\) It is the growth of abnormal cells capable of invading and destroying other associated skin cells\(^2\). Although each cell type in the skin is liable to give rise to a different type of neoplastic tumour, skin cancer is conveniently classified into non-melanoma skin cancers (NMSC) and melanoma.\(^1\) Melanoma is the most severe form of skin cancer.\(^3\) It is an aggressive and often fatal type of cancer that arises from transformed melanocytes (melanin producing pigments).\(^4\) The nonmelanoma group encompasses all other skin cancers and has a clinical course ranging from indolent to very aggressive form depending on the histology.

The two common forms of nonmelanoma skin cancer are the squamous cell carcinoma and basal cell carcinoma.\(^3\) The pattern of dermatological malignancies in Nigeria showed that squamous cell carcinoma is the most common histology type.\(^5\) This is in contrast to what is seen in Caucasian population in which 80% of the lesions are basal cell carcinoma (BCC) and 20% are squamous cell carcinoma (SCC).\(^6\) In an analysis of published literature on skin cancer in Nigeria, it was noted that the relative frequency of skin cancer is much lower than in White populations even though the incidence of skin cancer has continued to increase over the past decades.\(^7\) Skin cancer is ranked sixth in the top ten malignancies in Nigeria.\(^8\) Rare tumors include Merkel cell carcinoma (MCC), cutaneous connective tissue tumors such as dermatofibrosarcoma protuberans (DFSP), tumors of skin adnexa including eccrine and apocrine sweat gland and sebaceous carcinomas, tumors of cellular migrants to the skin such as mycosis fungoides. Skin Melanoma comprises only 3% of all skin cancers and accounts for about 75% of skin cancer mortality.\(^6\) Skin cancers occur more commonly in men than in women.\(^9\) Non melanoma skin cancer is commoner in middle aged and elderly though may present earlier in albinos.\(^10\) Melanoma has peak incidence fifth and sixth decades.\(^11\) The overall rate of skin cancer generally increases with age.\(^12\)

Currently, between 2 and 3 million non-melanoma skin cancers and 132,000 melanoma skin cancers occur globally each year. One in every three cancers diagnosed is a skin cancer and, according to Skin Cancer Foundation Statistics, one in every five Americans will develop skin cancer in their lifetime.\(^7\)
Basal cell carcinoma is commonest in the head and neck.\textsuperscript{13} Head region is also noted to be the most commonly affected site with squamous cell carcinoma in albinos.\textsuperscript{12}

The causes of skin cancers are multifactorial, including both environmental and host factors. The known environmental risk factors include sun exposure (ultraviolet (UV) light), chemical exposures and ozone depletion. Host risk factors include human papilloma virus, genetic susceptibilities, skin tone and immunosuppression.\textsuperscript{14} Kaposi sarcoma incidence has increased in Nigeria with the prevalence of human immunodeficiency virus (HIV).\textsuperscript{15,16} Most melanomas are believed to arise de novo, they also may develop from pre-existing benign nevi, especially those subject to repeated trauma and irritation.\textsuperscript{6} Skin cancers are a major risk associated with albinism and are thought to be a major cause of death in African albinos.\textsuperscript{10} Exposure to ultraviolet solar radiation, especially ultraviolet B (UVB; 290 to 320 nm), is the most common cause of skin cancer and the most preventable. Carcinogenesis results from ultraviolet solar radiation-induced DNA mutations in the \textit{p53} tumor suppressor gene and induction of immunologic changes that inhibit immune response against the tumor.\textsuperscript{6}

The Prospects of skin cancer depends on Breslow’s tumor thickness, Clark’s level of invasion, histological type, degree of histological differentiation of the tumour cells, clinical staging, primary site of tumour, age of patient, sex, co-morbid conditions and neuro-vascular invasion.\textsuperscript{17} Basal cell carcinoma are more aggressive in albinos.\textsuperscript{16}

Currently, the Gold standard of management of skin cancer is surgery. Chemotherapy and targeted therapies combined with radiation have shown improvement in patients overall survival.\textsuperscript{16} The purpose of this study is to evaluate the skin cancers and the outcome of treatment in patients with seen and managed in the Radiotherapy department from presentation to five years post treatment.
JUSTIFICATION

Skin cancer is a major public health problem with significant associated morbidity and mortality in both developing and developed countries. Though commoner in Whites, the prognosis is poorer in Blacks. The incidence is predominantly in the elderly age for BCC and SCC. With melanoma affecting both the young age and elderly and peak age of incidence is approximately 50 years, thus reducing the life expectancy of the population at risk as such it deprives the nation of skillful manpower and weakens the economy.

It is of considerable importance to the oncologist since it is the most accessible of cancers and tends to present early with over 90% cure rate in localized disease BCC and SCC. A reasonable number of patients still present late due to misdiagnoses, or delay while seeking alternative unorthodox medication, thereby presenting at advanced stage when the treatment is majority palliative.

Determining the outcome of treatments in patients will help the physicians in the proper decisions on the line of treatment and also enable patient or caregiver to be counselled appropriately on the possible outcome of the disease as life expectancy is less than 1 year in metastatic stage of melanoma. Albinos and others with predisposing factors to skin cancers will benefit from this study.
AIMS AND OBJECTIVES

General Objective

The aim of this project is to determine the outcome of treatments in patients with skin cancers seen at the Radiotherapy Clinic, University College Hospital, Ibadan between January 2001 and December 2010.

Specific Objectives

1. To determine the symptoms, presenting age and gender distribution, histological variants and frequencies of anatomical site affectations of skin cancers.
2. To determine the pattern of metastasis at presentation and during follow up.
3. To determine outcome of patients and overall survival following treatment.
4. To establish possible risk factors.
5. To compare and contrast the findings with those of previous studies both local and international studies.
LITERATURE REVIEW

The anatomy of the skin

The skin is the body’s largest organ, consists of the epidermis, a superficial cellular layer, and the dermis, a deep connective tissue layer. The epidermis, is a keratinized epithelium, that has a tough, horny superficial layer that provides a protective outer surface overlying its regenerative and pigmented deep or basal layer. The epidermis has no blood vessels or lymphatics. The avascular epidermis is nourished by the underlying vascularized dermis, which is supplied by arteries that enter its deep surface to form a cutaneous plexus of anastomosing arteries. The skin is also supplied with afferent nerve endings that are sensitive to touch, irritation (pain), and temperature. Most nerve terminals are in the dermis, but a few penetrate into the epidermis.\(^{12}\)

The skin represents the largest organ of the innate immune system, composing not only a physical barrier but also containing numerous elements important in the immunological response against invading pathogens.\(^{13}\) Like other complex organs, the skin is composed of several interdependent cell types and structures that are functionally cooperative and includes;

- **Squamous epithelial cells (keratinocytes)**, in addition to producing protective keratin protein, are major sites for the biosynthesis of soluble molecules (cytokines) that regulate adjacent epidermal cells as well as cells in the dermis.

- **Melanocytes**, within the epidermis are cells responsible for the production of melanin, a brown pigment that protects against potentially injurious ultraviolet (UV) radiation in sunlight.

- **Dendritic cells.** Skin is constantly battered with microbial and nonmicrobial antigens that are processed by intraepidermal dendritic Langerhans cells, which interact with the systemic immune system by migrating to regional lymph nodes.
- **Lymphocytes.** includes a subset of lymphocytes programmed to reside in the skin through expression of cutaneous lymphocyte-associated antigen. The local tissue response to cytokines produced by these T cells mediates the microscopic patterns and clinical expressions of cutaneous inflammatory and infectious disease.

- **Neural end organs** and **axonial processes** have recently been found to assist in regulation of immune competent cells, indicating important neuroimmune modulation. Among the neural network are neuroendocrine *Merkel cells* residing within the epithelial basal cell layer. These may serve as mechanoreceptors or possibly provide neuroendocrine function in skin.

- **Adnexal components.** Sweat glands guard against deleterious variations in body temperature, and hair follicles, in addition to manufacturing hair shafts, harbor protected niches of epithelial stem cells capable of regenerating superficial epithelial skin structures that have been disrupted by various hostile external and internal agents.

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**Epidemiology**

Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) of the skin are the most common cancers worldwide. Whites residing in locations with high exposure to ultraviolet (UV) radiation, such as Australia, and New Zealand and southern United States, have a particularly high lifetime risk for developing skin cancer. They are rare in dark-skinned races. BCC and SCC account for greater than 95% of non-melanoma skin cancer with BCC being four times more than SCC. They are markedly more common than malignant melanomas, which accounts for less than 5% of all skin malignancies.

Although NMSC does occur in younger people. Most BCCs and SCCs occur in individuals older than 50 years with fair complexions or outdoor occupations mostly on the sun-exposed head and neck or extremeties. The male to female ratio is 3:1 reflecting a greater tendency among men expose more to the sun. Cutaneous malignancies were most prevalent in the 6th and 7th decades of life with Melanomas being the most lethal of them, accounting for more than three quarters of all skin cancer deaths.
The incidence of melanoma has been increasing faster than any other cancer.\textsuperscript{16} Melanoma is affecting an increasingly younger population of adults, and even children, and is therefore a major threat to people in the most productive years of life. The incidence is 10 times greater in whites than in African Americans. Melanoma ranks as the seventh leading type of cancer in the United States. The estimated lifetime risk of developing melanoma in U.S whites is about 1 in 60.\textsuperscript{18}

As in many other countries with a predominantly white population, Skin tumours are the commonest of all neoplasms in the UK. In 2010, 12,818 people in the UK were diagnosed with malignant melanoma skin cancer with male: 6,201 and female: 6617. Also around 100,000 people were diagnosed with non-melanoma skin cancer with male: 55,609 and Female: 43,940. There were 2,746 deaths from skin cancer in the UK in the same year and around 2,203 from malignant melanoma skin cancer and 546 from non-malignant melanoma skin cancer. In 2005-2009, 84\% of men and 92\% of women in England survived their skin cancer for five years or more.\textsuperscript{19} This indicates a slight better prognosis in females.

Worldwide, the highest rates of malignant melanoma are in Australia and New Zealand\textsuperscript{19} Each year over 380,000 Australians are treated for skin cancer, outnumbering diagnoses of all other cancers combined\textsuperscript{20}. Two in every three Australians will develop some form of skin cancer during their lifetime\textsuperscript{21} and over 1,600 die from skin cancer each year\textsuperscript{22}. Gana et al in a study at Ibadan reported that commonest lesion recorded was squamous cell carcinoma accounting for 40.5\% of the cases. This was followed by malignant melanoma (25.1\%), dermatofibrosarcoma protuberance (9.5\%), Kaposi’s sarcoma 8.3\% and basal cell carcinoma (6.7\%). Less common histological types included adenocarcinoma, undifferentiated carcinoma, mucoepidermoid carcinoma, adenoid cystic carcinoma, fibrosarcoma and mycosis fungoides.\textsuperscript{23}

Ochicha et al.in a study in Northern Nigeria, reported that squamous cell carcinoma was the most common constituting 40\%, as in other Negroid populations, and melanoma the second most prevalent dermatological malignancy in their study constituting 34\% which is comparable to other Nigerian studies but relatively more than 5-10\% in Caucasians. Perhaps other non-pigment related genetic factors in Africans render us prone to SCC. BCC comprised only 4\% of skin cancers in this review. This is in marked contrast to 70-80\% in
Whites. The lower limbs were the most frequent site accounting for 70% of all malignant cutaneous neoplasms.

Seluye-Fubara et al. in a study at Port Harcourt, reported that Melanocarcinoma is rare in the environment total malignancies for the period under review. The age ranged from 39-76 years. Majority of the cases were female with F:M ratio of 3:2. The peak frequency of occurrence was among the age group 51-70 years. Only the nodular and the acral leniginous types were seen, of which the nodular type was the commonest. The feet and the legs were the commonest predilection sites while the head and neck as well as the knee were the least site of occurrence.

Though squamous cell carcinoma is still the leading cause of skin malignancy in Ibadan. There is a statistically significant decline in its proportion and a statistically significant increase in the proportion of basal cell carcinoma, compared to proportions documented three decades earlier. This change is due to subtle differences in aetiology. The proportion of Kaposi's sarcoma has also increased probably due to increasing HIV infection rate. The prevalence for basal cell carcinoma and malignant melanoma did not show the progressive increase in incidence noted among Caucasians.

Secondary deposits also occur in the skin. Risk of development of non-melanoma skin cancer depends on genotypic, phenotypic, and environmental factors. Risk is greatest in residents of high ambient solar irradiance who have markers of ultraviolet (UV) susceptibility, such as light skin, eye, and hair colour, or an inability to tan, and those with benign sun-related skin disorders—eg, actinic keratoses and solar lentigines. The finding that non-melanoma skin cancer occurs mainly on sun-exposed body sites and that its frequency can be reduced by sun protection provides indirect but crucial evidence for the role of ambient solar radiation.

The geographic variation in incidence of non-melanoma skin cancer is associated with ambient sun irradiance, providing further evidence for the relation between this disease and sun exposure. Incidence within countries is associated with increasing proximity to the equator. Gradients are similar for men and women, and all ages.
Worldwide, an estimated 46,000 people died from malignant melanoma in 2008. Almost 9 in 10 non-melanoma skin cancer deaths are in people aged 65 and over. Opara et al. reported that squamous cell carcinoma is the commonest non-melanotic skin cancer seen in albinos in eastern Nigeria. Amir et al. noted in the examination of the Tanzania Cancer Registry from 1978 to 1988 that squamous cell carcinomas was the most frequent form of superficial malignancy, followed by Kaposi’s sarcoma and then malignant melanoma. Males were also more afflicted than females, and the lower limbs were predominant sites of the lesion. In terms of relative importance of various types of superficial cancers, the pattern seen in Tanzania was similar to that in another East African country. In West African country, Kaposi’s sarcoma was not common. On the other hand, among blacks in the USA, basal cell carcinomas were almost similar in frequency to squamous cell carcinomas.

The percentage incidence of tumor types in epidermis and dermis.

### Cells of Epidermis and Respective Tumor Type

<table>
<thead>
<tr>
<th>Cells of epidermis</th>
<th>Tumor type</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanocyte</td>
<td>Melanoma</td>
<td>5-7</td>
</tr>
<tr>
<td>Epidermal basal cell</td>
<td>Basal cell carcinoma</td>
<td>60</td>
</tr>
<tr>
<td>Keratinocyte</td>
<td>Squamous cell carcinoma</td>
<td>30</td>
</tr>
<tr>
<td>Merkel cell</td>
<td>Merkel cell tumor</td>
<td>1-2</td>
</tr>
<tr>
<td>Langerhans cell</td>
<td>Histiocytosis X</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Appendage cells</td>
<td>Appendageal tumors</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

### Cells of Dermis and Respective Tumor Type

<table>
<thead>
<tr>
<th>Cells of dermis</th>
<th>Tumor type</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibroblast</td>
<td>Benign and malignant fibrous histiocytic tumors</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Mast cell</td>
<td>Mast cell tumor</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Vasculature</td>
<td>Angioma and angiosarcoma</td>
<td>&lt;1</td>
</tr>
<tr>
<td></td>
<td>Lymphangioma</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Lymphocyte</td>
<td>Non-hodgkins lymphoma</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>
Aetiological factors

The causes of NMSC are multifactorial, including both environmental and host factors. Sunlight is the main environmental cause of skin cancer. The sun emits a wide variety of electromagnetic radiation, including infrared, visible, ultraviolet A (UVA; 320 to 400 nm), ultraviolet B (UVB; 290 to 320 nm), and ultraviolet C (UVC; 10 to 290 nm). The only UVR wavelengths that reach the Earth's surface are UVA and UVB.

Farmer et al. reported that the depth to which UVR penetrates the human skin also is wavelength dependent. UV has the potential to penetrate the epidermis and upper layer of the dermis, or papillary dermis. Although UVB makes up only 5% of the UV photons reaching the earth’s surface, it is the most biologically important component of sunlight. UVA, with the longest wavelength, reaches the deeper layer of the dermis, or reticular dermis. UVB is considered to be the major cause of skin cancer despite its not penetrating the skin as deeply as UVA or reacting with the epidermis as vigorously as UVC. UVB’s reactivity with macromolecules combined with depth of penetration make it the biologically most potent portion of the UV spectrum, with respect to short-term and long-term effects. UVA, while possibly not as dangerous, also induces biological damage. UVA radiation is 1,000-fold less effective than UVB in producing skin damage. However, its predominance in the solar energy reaching the Earth's surface (tenfold to one hundredfold more than UVB) permits UVA to play an important role in contributing to the harmful effects of sun exposure than previously suspected. Excess exposure to ultraviolet radiation, particularly early in life is strongly associated with subsequent risk of developing melanoma. A history of sunburn or intense intermittent exposure may be particularly relevant.

Diffey reviewed epidemiological studies in an association between melanoma and sunlight exposure and reported that it does not appear that cumulative sun exposure explains the relationship, as it does for NMSC. Instead, an intermittent exposure hypothesis proposes that infrequent intense exposure of unacclimatized skin to sunlight is related to increasing melanoma incidence and is more important than chronic sun exposure. This hypothesis is
supported by the observation that most studies have shown that an increased risk of melanoma is associated with a past history of severe sunburn in childhood and adolescence.\textsuperscript{35}

The exposed skin surface of individuals is irradiated differently depending on cultural and social behaviour, clothing preferences and the position of the sun in the sky relative to the body. The power of irradiation depends on many environmental factors: solar UVR is strongest at noon (the point halfway between sunrise and sunset), when the sun is at its highest in the sky. UVR is strongest at the equator; at higher latitudes, the sun is lower in the sky resulting in lower UVR levels. UVR intensity increases as altitude increases\textsuperscript{36}

Artificial exposure to ultraviolet (sunbed) radiation has also contributed to the increased incidence of melanoma over the past decade. Indoor tanning exposes users to both UVA and UVB rays, which damage the skin and can lead to cancer. Using a tanning bed is particularly dangerous for younger users; people who begin tanning younger than age 35 have a 75\% higher risk of melanoma.\textsuperscript{37}

The effects geographic Differences have been noted. Whiteman et al. examined evidence from migrant studies and found that as people migrated from countries with low ambient solar radiation to countries with high solar UV at successively older ages, their melanoma risk decreased compared with those who arrived in early childhood (younger than 10–15 years). On the other hand, those who migrated in very early childhood from countries with high to those with low ambient exposure, were at similar risk of melanoma to native-born residents after living at least a year at the low latitude. thus supporting the notion that childhood is a susceptible period for UV carcinogenesis.\textsuperscript{38}

Chemical skin cancer carcinogens include arsenic, soot, and polycyclic aromatic hydrocarbons from coal tar, cutting oils, and pitch.\textsuperscript{39} Arsenical exposure predisposes to the development of Bowen’s disease, multiple BCC, and SCC, and is also associated with a higher incidence of intestinal carcinoma. Hard, yellowish hyperkeratotic plaques on the palms and soles provide a clue that the patient was exposed to arsenic.\textsuperscript{40}

Host risk factors include blonde or red hair, fair complexion, blue eyes, and tendency to burn rather than tan as well as the genetic predispositions occurring with xeroderma
pigmentosum, basal cell nevus (Gorlin's) syndrome, epidermodysplasia verruciformis, Muir-Torre syndrome, porokeratosis, Bazex syndrome, Rombo syndrome, albinism, and phenylketonuria. An association exists between cutaneous SCC and human papillomavirus.\textsuperscript{5}

The p53 gene and the patched gene (PTCH) are major targets of UV for BCC induction. Mutations in p53 are present in about 56\% of human BCC. Mutations in the PTCH play also a major role in BCC development, being responsible for hereditary BCCs in Gorlin's syndrome, sporadic BCC, and BCCs isolated from xeroderma pigmentosum. Smoothened-activating mutations and PTCH2 mutations are also involved in BCC formation.\textsuperscript{41}

Genetic risk is considered very important in the aetiology of melanoma as 10\% of cases will have a strong family history of melanoma. Germline mutations are implicated in up to 40\% of patients with familial melanoma and have a role in sporadic cases.\textsuperscript{32} Individuals with xeroderma pigmentosum have a rare genetic DNA defect in repair of ultraviolet light damage and are at a considerable increased risk for developing skin cancer. Kraemer et al noted that the median age of first nonmelanoma skin cancer among patients with xeroderma pigmentosum was 8 years, more than 50 years less than that among patients with skin cancer in the United States.\textsuperscript{42}

Oncogene (\textit{Ha-ras, Ki-ras, N-ras, c-myc}, and others) mutation and amplification, as well as anti-oncogene \textit{p53} mutations, have been reported for BCC and SCC.\textsuperscript{40} Benign pigmented naevi may be precursor lesions to malignant disease. Tucker et al noted that the risk for melanoma was strongly related to number of small nevi, large nondysplastic nevi, and clinically dysplastic nevi.\textsuperscript{43} Also that the presence of a single dysplastic nevus results in a 2.3-fold increased risk for melanoma, whereas having more than five lesions leads to a more than tenfold increased risk for developing melanoma.\textsuperscript{43}

Transplant recipients on immunosuppressive therapy and patients with acquired immunodeficiency syndrome, multiple myeloma, leukemia, and lymphoma also are at increased risk. Skin cancers are more frequent and aggressive in areas of chronic skin damage such as ulcers, osteomyelitis, sinus tracts and burn (Marjolin's ulcer), or vaccination scars. Areas of chronic skin inflammation such as discoid lupus erythematosus, lichen sclerosus, lichen planus, dystrophic epidermolysis bullosa, and lupus vulgaris also are predisposed to develop skin cancers.\textsuperscript{5} Exposure to ionizing radiation is a risk factor for both
BCC and SCC, especially in those people with sun-sensitive phenotype and younger age at exposure. Lesions develop within the radiated area with latency periods of 20 to 40 years, and risk is directly related to cumulative radiation dose.

An association exists between cigarette or pipe smoking and cutaneous SCC, with risk proportional to the number of cigarettes or pipes smoked daily and higher in current rather than former smokers.

**Pathogenesis**

The exact genetic alterations and numbers of mutations needed for malignant transformation are yet unknown. The most readily accepted theory involves the transformation of the epidermal p53 gene clones by ultraviolet (UV) exposure to the precursors of squamous cell carcinoma. Early p53 mutations are believed to inhibit apoptosis of abnormal cells, allowing them to expand at the expense of normal presenting cells. Alterations of the p53 gene are the most common presenting malformation in all stages of squamous cell carcinoma, starting at the precancerous lesion and advancing to the invasive and potentially metastatic forms. Genetic alterations within the p53 gene have been shown to have a direct correlation with cancer development and have been shown to occur in nearly 50% of all cancers.

UVR damage to biological systems occurs via phototoxic reactions that are either direct or mediated by photosensitizers in the target tissues. In the skin, the effects of UVR are mediated by photosensitization reactions characterized by structural and functional changes in keratinocytes, melanocytes, Langerhans cells, and fibroblasts. The mechanism of UVR-induced DNA damage differs distinctly with wavelength. The depth to which UVR penetrates the human skin also is wavelength dependent. The atmosphere filters out UVC, the shortest wavelength produced by sunlight and the most potentially harmful to the genome, before it reaches the earth’s surface. Therefore, UVC plays only a minimal role in biological photochemical reactions. UVC produced by artificial sources and reaching the skin can penetrate only the epidermis. UVB has the potential to penetrate the epidermis and upper layer of the dermis, or papillary dermis. Although UVB
makes up only 5% of the UV photons reaching the earth’s surface, it is the most biologically important component of sunlight.\textsuperscript{48}

UVA, with the longest wavelength, reaches the deeper layer of the dermis, or reticular dermis. UVA is less mutagenic than is UVB, and causes indirect DNA damage via a photo-oxidative-stress-mediated mechanism, resulting in formation of reactive oxygen species, which interact with lipids, proteins, and DNA to generate intermediates that combine with DNA to form adducts.\textsuperscript{49} UVA is hardly able to excite the DNA molecule directly and produces only few pyrimidine dimers. Oxidative DNA base damage, generated indirectly through photosensitizers, might be responsible for the mutagenic and carcinogenic properties of UVA.\textsuperscript{50}

Farmer et al noted that UVB is considered to be the major cause of skin cancer despite its not penetrating the skin as deeply as UVA or reacting with the epidermis as vigorously as UVC. UVB’s reactivity with macromolecules combined with depth of penetration make it the biologically most potent portion of the UV spectrum.\textsuperscript{51} Damage to DNA by UVA proceeds indirectly via photosensitizers (non-DNA molecules) in photosensitization reactions, because DNA does not readily absorb UVA. In contrast, wavelengths shorter than 320 nm (UVB, UVC) directly photoactivate the DNA molecule to generate mainly pyrimidine photoproducts.\textsuperscript{48} UVB radiation causes direct damage to DNA and RNA by inducing covalent bond formation between adjacent pyrimidines, leading to generation of mutagenic photoproducts such as cyclopyrimidine dimers (TT) and pyrimidine-pyrimidine.\textsuperscript{52}

Melanoma occurs when unrepaired DNA damage to skin cells (most often caused by ultraviolet radiation from sunshine or tanning beds) triggers mutations, or genetic defects, that lead the skin cells to multiply rapidly and form malignant tumors.\textsuperscript{53} Lower levels of oncoprotective cutaneous melanin in Caucasians render them more vulnerable to carcinogenic solar ultra violet (UV) radiation particularly from recreational sun exposure.\textsuperscript{8} A previously unrecognized herpesvirus—human herpesvirus-8 (HHV-8) or KS-associated herpesvirus (KSHV) was identified in a cutaneous KS lesion in an AIDS patient in 1994.\textsuperscript{14} Cytokines derived from HIV-infected T cells, or inflammatory cells recruited in response to the lytic infection, create a local proliferative milieu; a virally encoded G protein also induces
local VEGF production, targets. KSHV induces a lytic as well as a latent infection in endothelial cells, both of which are probably important in KS pathogenesis.

**Pathology**

Skin cancer is conventionally classified into melanoma and nonmelanoma. BCC and SCC are by far the most frequent types of nonmelanoma skin cancers, approximately 82 types of skin malignancies, with a wide range of clinical behaviors, fall into the category of nonmelanoma skin cancer. Other types of nonmelanoma skin cancers include the following:

- Cutaneous T-cell lymphomas (e.g., mycosis fungoides).
- Kaposi sarcoma
- Extramammary Paget disease.
- Apocrine carcinoma of the skin.
- Metastatic malignancies from various primary sites

**Melanoma; Histopathologic types**

**Superficial spreading melanoma** (SSM) or radial spreading melanoma is the most common type accounting for 70% of melanomas. It is commonly found on the trunks of men and lower extremities of women. The lesion is a pigmented macule or a barely palpable plaque with variegated colors and irregularity of the margins. These tumors mostly manifest radial growth but eventually enter a vertical growth phase.

**Nodular melanoma** (NM) comprises of 10% to 15% of melanomas and has an early vertical growth phase. It is commonly found in the trunks of men. NM often presents as a brown-black papule that may ulcerate and grow rapidly. It may occasionally present with no pigment (amelanotic) and a distinct border. They may not be detected early. This may explain why these lesions are often thicker at initial presentation, which leads to a worse prognosis.

**Lentigo maligna melanoma** accounts for approximately 10% of melanomas. It has no sexual predilection. It is characterized by flat, large (1 to 5 cm) lesions located on the arms, hands and the face of the elderly (median age of 70 years) in particular developing in sun-exposed areas of older, light-skinned people. The *in situ* lentigo maligna lesion shows a
horizontal growth phase for up to 20 years and eventually a vertical growth phase anywhere in the involved area.

**Acral lentiginous melanoma** is seen in approximately 3% to 5% of melanoma and occurs primarily on the palmer surfaces of the hands, plantar surfaces of the feet, and under nails, on the digits. This melanoma subtype is most commonly seen in individuals with darker-pigmented skin.

**Unclassified** and rare desmoplastic variants also exist.\(^6,40,56\)

**Basal cell carcinoma (BCC) ; Histopathologic types**

BCC is an epithelial malignant tumour with a low malignant potential, consisting of cells which look like the basal epidermis layer. The diagnostic histological features, common for all types of the tumour, are basaloid cells with a thin pale cytoplasm surrounding round or oval nuclei with a rough granulated chromatin pattern. The peripheral borderline cell layers are characterised by palisade arrangement and the surrounding stroma is often separated by artificially created slits, whereas the internal arrangement of the cells is rather chaotic. Most tumours originate in the epidermis and invade the dermis in the form of solid or cystic nodules or streaky projections creating various growth pattern.\(^57\)

They include nodular, pigmented, micronodular, cystic, morpheaform (sclerosing), superficial, linear, infiltrative.\(^1,15,61\)

**Nodular BCC** - This tumour starts as a small papule which subsequently becomes nodular, that may develop central umbilication and undergoes central ulceration as lesion grows. The margins are well defined, slightly raised with a rolled borders and a pearly shiny appearance. It is composed of discreet islands of darkly staining cells with uniform nuclei and scanty cytoplasm with typically peripheral palisading pattern. It is the commonest variety. This is also known as rodent ulcer.

**Pigmented BCC** - This type of BCC is clinically similar to the nodular BCC but the margins of the tumour are pigmented. Such pigmented BCC may easily be mistaken clinically for melanoma.

**Cystic BCC** - This is a well defined papule which attains a pearly coloured lobulated appearance with a telangiectic surface. The hallmark of this tumour is the presence of cystic foci creating a lace like appearance of darkly staining cells.
Morphoeic (sclerosing) BCC – This is a rare variety. It appears as plaque of scar-like tissue (scleroderma) with an ill-defined border making the diagnosis difficult and often late. They are flat and detection depends on how much fibrosis of they contain. Clinically recognition is assisted by stretching the skin or pressing it with a glass. They spread lateral rather than deep and occur virtually exclusive on the face\textsuperscript{1,15,61}

Superficial BCC - manifests as red, scaly macules with indistinct margins, usually located on the trunk. They are round or oval. Sometimes the border is scalloped or ill defined. The tumour can sometimes be discontinuous or multicentric, so surgical excision sometimes leaves some tumor behind. Histologic examination shows multiple foci of buds of neoplastic cell with peripheral palisading originating from the undersurface of the epidermis.\textsuperscript{61}

Linear BCC - This is an uncommon variant of BCC Clinically it is a linear, pearly and telangiectatic lesion and is located most often on the head and neck. It belongs to a more aggressive subtype and is more likely to have subclinical spread

Infiltrative BCC - It has an opaque yellowish appearance and blends subtly with the surrounding skin. Histologically, the lesion is characterized by poorly circumscribed spiky cell aggregates in the superficial portion and the main bulk, consisting of strands of neoplastic cells infiltrating the reticular dermis and subcutis.\textsuperscript{1,57}

**Squamous cell carcinoma (SCC); Histopathologic types**

This is also known as epidermoid, spindle cell or prickle cell carcinoma. It is a malignant tumour that arises from epithelial keratinocytes whose cells usually show some degree of maturation toward keratin formation. Pathological variants include hypertrophic, atrophic, acanthotic, Bowenoid and pigment types. The characteristics of all these pathological subtypes are atypical keratinocyte proliferation within the epidermis. The atypical keratinocytes themselves show loss of polarity, nuclear pleomorphism, disordered maturation and increased numbers of mitotic figures.

Clinically, SCC in situ (Bowen’s disease) manifests as a soft, erythematous, scaly, well-circumscribed patch. Superficial carcinoma manifests as a scaly, crusted plaque or ulcer with a verrucous or papillate border, and infiltrating SCC manifest as a firm, ulcerated mass with an elevated nodular border. Invasive SCC consist of irregular masses, composed of a mixture of anaplastic and differentiated squamous cells, growing downwards into the dermis.
from the epidemis. Histologically, SCC is graded as well, moderately, or poorly differentiated, based on the magnitude of tumour of cellular polymorphism, keratinization, and mitosis.\(^1,15\)

**Kaposi sarcoma (KS)**

This is common in patients with AIDS; indeed, its presence is used as a criterion for diagnosing AIDS.

**Histopathologic types:** Four forms of the disease are recognized

- *Chronic KS* (also called *classic* or *European KS*). It characteristically occurs in older men of Eastern European (especially Ashkenazi Jews) or Mediterranean descent and is uncommon in the United States. While chronic KS can be associated with an underlying second malignancy or altered immunity, it is not associated with human immunodeficiency virus (HIV). Chronic KS presents with multiple red to purple skin plaques or nodules, usually in the distal lower extremities; these slowly increase in size and number and spread more proximally. Although locally persistent, the tumors are typically asymptomatic and remain localized to the skin and subcutaneous tissue.

- *Lymphadenopathic KS* (also called *African* or *endemic KS*). It is particularly prevalent among South African Bantu children; it is also not associated with HIV. Skin lesions are sparse, and patients present instead with lymphadenopathy due to KS involvement; the tumor occasionally involves the viscera and is extremely aggressive. In combination with AIDS-associated KS, KS is now the most common tumor in central Africa (50% of all tumors in men in some countries).

- *Transplant-associated KS* occurs in the setting of solid-organ transplantation with its attendant long-term immunosuppression. It tends to be aggressive with nodal, mucosal, and visceral involvement; cutaneous lesions may be absent. Lesions occasionally regress when immunosuppressive therapy is attenuated, but at the risk of organ
rejection.

- **AIDS-associated (epidemic) KS** was originally found in a third of AIDS patients, particularly male homosexuals. However, with current regimens of antiretroviral therapy, KS incidence is now less than 1%. AIDS-associated KS can involve lymph nodes or viscera and disseminates widely early in the course of the disease. Most patients eventually die of opportunistic infections rather than from KS.14

**Other vascular tumours**

*Hemangioendothelioma* denotes a wide spectrum of vascular neoplasms with clinical behaviors intermediate between benign, well-differentiated hemangiomas and highly malignant angiosarcomas.

*Epithelioid hemangioendothelioma* is an example; it is a vascular tumor of adults occurring around medium-sized and large veins. The tumor cells are plump and often cuboidal (resembling epithelial cells); well-defined vascular channels are inconspicuous. Clinical behavior is variable; most are cured by excision, but up to 40% recur, 20% to 30% eventually metastasize, and perhaps 15% of patients die of the tumors.

*Angiosarcomas* are malignant endothelial neoplasms with histology varying from well-differentiated tumors that resemble hemangiomas (*hemangiosarcoma*) to anaplastic lesions difficult to distinguish from carcinomas or melanomas. Older adults are more commonly affected, with equal gender predilections; they occur at any site but most often involve skin, soft tissue, breast, and liver.14

MCC is malignant neuroendocrine cells. Recent studies have shown that MCC shares pathogenetic mechanisms with other neoplasms of neural crest derivation such as malignant melanoma and neuroblastoma. Merkel cells are specialized sensory cells present in the basal or suprabasal layers of the epidermis .58

MCC resembles malignant melanoma in several ways. Both have an unpredictable biological behaviour, early regional lymph node involvement, early distant metastases, and high
recurrence rate. MCC is a small cell cutaneous malignancy that often manifests as a rapidly enlarging firm, painless, pink-red, dermal-based nodule, most frequently on the head and neck or extremities in older (>60 to 70 years old) individual.\textsuperscript{15}

**Adnexal Carcinoma**

Sebaceous carcinomas are rare and arise most commonly (75\% of cases) from the sebaceous glands of the ocular adnexa, Sebaceous carcinoma differentiated from the epithelium lining of the sebaceous gland. Depending on the sites of occurrence, it is classified into ocular sebaceous carcinoma and extraocular sebaceous carcinoma constituting the remaining 25\%.\textsuperscript{59} Extraocular locations, in decreasing frequency, are head and neck region, trunk and extremities, and external genitalia. Histologically, these carcinomas are composed of dermal-based lobules and cords of tumor cells, with varying degrees of sebaceous differentiation and infiltration into surrounding tissues.\textsuperscript{15}

**Eccrine Carcinoma:**

Sweat gland (eccrine, apocrine, apoeccrine) carcinomas are exceedingly rare, arise most frequently in the skin of the head and neck or extremities, and manifest as painless papules or nodules that grow slowly. This type of neoplasm is usually diagnosed in individuals 50 to 70 years of age. Histologically, eccrine or sweat gland carcinomas may resemble carcinomas of the breast, bronchus, and kidney and are difficult to differentiate from cutaneous metastases.\textsuperscript{15} In addition to the eccrine and apocrine glands, two other skin sweat glands have recently been described: the apoeccrine and the mammary-like glands of the anogenital area.\textsuperscript{60}

**Microcystic Adnexal Carcinoma**

Microcystic Adnexal Carcinoma is a rare locally aggressive carcinoma that belongs to the spectrum of adnexal carcinomas and most often arises on the head and neck. It usually grows slowly over years and often is deeply invasive when diagnosed.
Histologically, the tumor is composed of keratin horn cyst, nests, or cords of basaloid cells that are usually more prominent in the superficial dilated tubes are arranged in solid islands and embedded in deeper desmoplastic stroma.\textsuperscript{15}

**Tumors of Cellular Migrants to the Skin**

Aside from tumors that arise directly from epidermal and dermal cells, several proliferative disorders of the skin involve cells whose progenitors arise elsewhere and home to the cutaneous microenvironment.

**Mycosis fungoides (cutaneous T-cell lymphoma)**

Mycosis fungoides is a T-cell lymphoma that presents in the skin and may evolve into generalized lymphoma. Most affected individuals have disease that remains localized to the skin for many years; a minority have rapid systemic dissemination. This condition may occur at any age, but most commonly it afflicts persons older than age 40. Lesions of mycosis fungoides usually involve truncal areas and include scaly, red-brown patches; raised, scaling plaques that may even be confused with psoriasis; and fungating nodules. Prognosis is related to the percentage of body surface involved and progression from patch to plaque to nodular forms. Eczema-like lesions typify early stages of disease when obvious visceral or nodal spread has not occurred.\textsuperscript{14}

**Secondary deposits to the skin**

Malignant skin lesions can metastases from other organs, e.g. from breast, lung, or gastrointestinal primaries.\textsuperscript{32}

**Staging**

The current UICC staging of melanoma divides the tumour into four stages.

**Stage 1:** tumours less than 1.5 mm thick

**Stage 2:** primary tumour thicker than 1.5 mm

**Stage 3:** tumour spread to the local draining lymph nodes
Stage 4: distant disease

Prognosis for patients with Stage 3 and 4 disease is poor, with only 25% disease-free two-year survival for Stage 3 and around 6% two year survival for Stage 4.\textsuperscript{32}

TNM system for classification of cutaneous carcinomas uses NX, N0, or N1 for unassessed, absent, or present regional lymph node metastasis, respectively, and MX, M0, or M1 for unassessed, absent, or present distant metastasis, respectively.

Primary tumor stage

TX Primary tumor cannot be assessed
T0 No evidence of primary tumor
Tis, pTis Carcinoma \textit{in situ}
T1, pT1 Tumor 2 cm or smaller in greatest dimension
T2, pT2 Tumor 2 to 5 cm in greatest dimension
T3, pT3 Tumor more than 5 cm in greatest dimension

The histopathologic grades for cutaneous carcinomas are as follows:
GX Grade cannot be assessed
G1 Well differentiated
G2 Moderately differentiated
G3 Poorly differentiated
G4 Undifferentiated

Clark Method of Microstaging (Level of Invasion)

Clark Level

- Melanoma limited to the epidermis
- Invasive melanoma with superficial infiltration to the papillary dermis
- Melanoma extending to the superficial vascular plexus in the dermis
- Primary melanoma involving the reticular dermis
- Melanoma involving the subcutaneous fat.
Natural history

**Melanocytes** are believed to migrate from the embryonic neural crest to the dermal-epidermal junction of the skin. The number of melanocytes per unit of skin surface appears to be the same for all races, even albinos. Pigmentary differences between races are dependent on how the melanin is “packaged” in each cell.

**Mode of spread.** Most cutaneous melanomas are believed to arise near the basal lamina.

a. **Radial growth.** The superficial spreading and lentigo maligna melanomas grow horizontally along the lamina (radial growth phase) before penetrating the deep skin structures (vertical growth phase). The radial phase may last as long as 20 years in lentigo maligna and 5 years in superficial spreading melanoma.

b. **Vertical growth.** Nodular melanomas have a vertical growth phase from the outset. The vertical phase is associated with invasion of dermal blood and lymphatic vessels.

c. **Lymphatics.** Local lymphatic spread results in satellite nodules of melanoma appearing near the site of the primary tumor (*satellitosis*). Draining lymph nodes are frequently involved after the vertical growth phase develops. The first lymph node to become involved is termed the *sentinel node*.

d. **Distant metastases.** Metastatic melanomas can involve any organ in the body, including the placenta and fetus. About 5% of patients with melanoma present with symptoms of distant metastases without an apparent primary site.

Basal cell carcinoma tend to more indolent and rarely metastasize. The biologic behavior varies with the histologic type. A superficial BCC may remain stable for a long time or enlarge gradually over years. Morpheaform, infiltrating type are more aggressive variants that may spread through peripheral invasion or infiltration of deeper structures.

Squamous cell carcinoma has a more aggressive course than BCC. Carcinoma in situ (or Bowens disease) may evolves gradually into superficial carcinoma in 5% of cases. Untreated, it may progress further into an infiltrating type that invades the surrounding and overlying structures.
**Clinical presentation**

**Melanoma**

Primary melanoma of the skin presents as a growing, irregular brown or black lesion on the skin. Important features to alert clinical suspicion include an irregular outline to the lesion; irregular pigmentation containing shades of brown, black, and red; and, occasionally, oozing crusting. They may arise on previously normal skin or on a previously apparently benign melanocytic naevus.\(^3^2\)

The Features of Familial Melanoma include: Multiple melanomas, Melanoma at young age, Melanoma often associated with dysplastic nevi.

The clinical features “ABCDE” suspicious for melanoma are as follows:

A; Asymmetry of a lesion,

B; Borders that are irregular,

C; Colour that is multihued,

D; Diameter greater than 6mm

E; Evolving changes in the lesion over time\(^6^3\)

Other characteristics of concern could include history of recent growth, ulceration, itching or bleeding. The nonpigmented skin lesions that behave like melanoma should be examined with the immunochemical stains S-100 and HMB -45 as 1% to 2% of melanoma lesions are amelanotic.\(^6^3\) The clinical pathologic features of melanoma vary with the anatomic site in which it originates. Data from genetic analyses have confirmed the existence of distinct subtypes with characteristic genetic alterations depending on anatomic site and degree of sun-exposure.\(^6^4\) Thus although melanomas are commoner in Whites the prognosis is poorer in Blacks.\(^8\)
### Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Basal cell carcinoma</th>
<th>Squamous cell carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>Most common cancer of the skin in whites</td>
<td>Next most common skin cancer in whites</td>
</tr>
<tr>
<td>Cell of origin</td>
<td>Basal cells of epidermis and hair follicles</td>
<td>Epidermal keratinocytes</td>
</tr>
<tr>
<td>Site of tumor</td>
<td>Sun-exposed areas of head and neck, ear, and extremities</td>
<td>Sun-exposed areas of head, neck, face, for and dorsum of the hand</td>
</tr>
<tr>
<td>Ethnic background</td>
<td>Fair skin</td>
<td>Fair skin</td>
</tr>
<tr>
<td>Sun exposure</td>
<td>Continuous cumulative exposure</td>
<td>Continuous cumulative exposure</td>
</tr>
<tr>
<td>Male/female ratio</td>
<td>Common in men</td>
<td>Common in men</td>
</tr>
<tr>
<td>Growth and</td>
<td>Slow growing and good prognosis</td>
<td>Slow growing and good prognosis</td>
</tr>
<tr>
<td>prognosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mucosal origin</td>
<td>None</td>
<td>Involves lip and mouth</td>
</tr>
</tbody>
</table>

### Diagnosis

The key to evaluation of suspected lesions focuses on obtaining a full-thickness biopsy. Excisional biopsy is the best choice for small lesions or for large lesions in cosmetically favorable locations. Excisional biopsy should extend down to the subcutaneous fat, with a small (2-3mm) peripheral margin. Punch biopsy can be performed for large lesions or for lesions with a low suspicion of melanoma in a cosmetically unfavorable location. The biopsy should be performed at the highest or thickest point of the lesion. Incisional biopsy is not recommended. Likewise, other techniques that do not permit a full-thickness sample, such as shave or curette biopsy, are discouraged.65,66

Laboratory tests are usually not required for the diagnosis and evaluation of basal and squamous cell carcinoma. However, for locally advanced diseases CT scan or MRI for evaluating the depth of invasion and regional lymph node is indicated especially in melanoma that usually spreads to distant sites.66

CT scans of the chest are useful for evaluating suspected pulmonary, pleural, or mediastinal metastases.67
Treatment

Treatment is dependent on type of cancer, location of the cancer, age of the patient, and whether the cancer is primary or a recurrence. Treatment is also determined by the specific type of cancer. For a small basal cell cancer in a young person, the treatment with the best cure rate (Mohs surgery) might be indicated. In the case of an elderly frail man with multiple complicating medical problems, a difficult to excise basal cell cancer of the nose might warrant radiation therapy (slightly lower cure rate) or no treatment at all. Topical chemotherapy might be indicated for large superficial basal cell carcinoma for good cosmetic outcome, whereas it might be inadequate for invasive nodular basal cell carcinoma or invasive squamous cell carcinoma. Optimal surgical margins depend on the thickness of the primary lesion.68

Surgical Treatment of Primary Melanoma

Surgical excision continues to be the mainstay in the treatment of primary melanoma and consists of resecting the intact tumor or biopsy site en bloc with a surrounding margin of normal-appearing skin and underlying subcutaneous tissue. The goals of surgical treatment are to remove all the melanoma cells at the primary site to provide durable local disease control for all patients, even when the likelihood for distant relapse is high, and to effect a cure in those patients at low risk of harboring occult metastatic disease. Without compromising these goals, efforts should be made to carry out the surgical excision in a manner that minimizes costs, functional impairment, and cosmetic disfigurement.66

Complete surgical excision of the primary melanoma, confirmed by comprehensive histologic examination of the entire excised specimen, forms the basis for surgical treatment of primary melanoma.18 Local excision of early melanoma is the only proven method of curative therapy. The extent of tumor-free margins that is necessary remains controversial. Current required surgical margins are 5 mm for in situ lesions, 1 cm for thin melanomas (1 mm or smaller), and 2 to 3 cm for lesions thicker than 1 mm.40 Eggermont, in a study show that a 1 cm margin is sufficient for melanomas < 2 mm and that a margin of 2 cm is adequate for melanomas 1–4 mm.69 Heaton et al. in another study
demonstrated a lack of impact of wider than 2 cm excision margins on the local recurrence rate, disease free survival and overall survival in patients with melanomas thicker than 2 mm. Taken together, it shows that a 2 cm margin can be considered adequate for all melanomas thicker than 2 mm. This means that virtually all melanomas at any site can be treated by excision and primary closure.\textsuperscript{70}

Mohs micrographic surgery should be considered for facial melanoma and other areas where tissue conservation is desired because of its equivalent cure rate. Tumor margin is often influenced by site. Large defects may require skin grafting or skin flaps.\textsuperscript{40}

**BCC and SCC**. For most BCC or SCC lesions, surgical treatments or radiation therapy offer equivalent excellent cure rates of 90\% to 95\%. However, treatment approach must be individualized based on specific risk factors and patient characteristics for the most acceptable cosmetic and functional outcome.\textsuperscript{5}

**Traditional surgical resection** requires a surgical margin of 4 to 6 mm for primary tumors less than 2 cm in diameter (more margin for bigger primary tumors, tumors in high-risk areas, or recurrent tumors). Lack of complete visualization of tumor margins because of sampling error may result in tumor recurrence.

**Mohs micrographic surgery** This is a specialized technique used with the intent to achieve the narrowest margins necessary to avoid tumor recurrence, while maximally preserving cosmesis. Mohs micrographic surgery requires special training. The tumor is microscopically delineated, with serial radial resection, until it is completely removed as assessed with real-time frozen sections.\textsuperscript{71}

It has the highest cure rates, maximally spares uninvolved tissue, and is less costly than radiation therapy. This procedure is more often used in the treatment of basal cell carcinomas.\textsuperscript{72}

Mohs surgery is indicated for the following lesions:

- Located in regions at high risk for tumor recurrence (i.e., the periorbital area, nasolabial fold, nose–cheek angle, posterior ear sulcus, pinna, ear canal, nose, forehead, and scar tissue)
- Located in regions where tissue conservation is mandated
- Poorly defined clinical borders
- Diameter greater than 2 cm
- Perineural invasion
- Morpheaform, sclerotic, infiltrating, micronodular, or basosquamous histopathologic features or linear clinical presentation
- Recurrent BCC or SCC. Of all therapeutic modalities for recurrent tumors, Mohs surgery has the greatest success rate (95%) and should ordinarily be considered the preferred treatment.  

**Curettage** of the tumor with electrodesiccation of the apparently normal base to an additional depth of 3 or 4 mm is particularly useful for superficial BCC of the trunk or Bowen’s disease.

**Cryosurgery** using liquid nitrogen to freeze the tumor to –40°C should be considered for patients who refuse surgery or are poor surgical candidates. A probe to monitor freezing must be used for all tumors with the possible exception of superficial BCC. Cryosurgery is contraindicated for sclerosing BCC and cold-induced diseases.

**Lymph Node Dissection**

Invasion of the lymphatics by a vertically growing melanoma causes the tumor to lodge in the local lymph node basin. The tumor, uninterrupted at this lymph node basin, may spread to deeper lymphatics or hematogenously to systemic organs. This principle forms the rationale for complete surgical resection of the tumor from the lymph node basin before the tumor spreads to distant organs, and is considered a potentially curative procedure.  

**Surgical Approach to Obtain a Sentinel Lymph Node**

Preoperative lymphoscintigraphy uses vital blue dye and provides a road map of the lymph node basin. Intraoperative lymphoscintigraphy uses radiocolloid injection around the primary tumor, and a gamma camera detects the radioactivity from the involved lymph node, thereby acting as a navigator to the involved lymph node. The combination of vital blue dye and technetium-labeled sulfur colloid identifies the sentinel lymph node in 94% of cases.
**Isolated Limb Perfusion**

Principle: To deliver maximally tolerated chemotherapy doses to a regionally confined tumor area while limiting systemic toxicity. Hyperthermia and oxygenation of the circulation potentiate the tumoricidal effects of the chemotherapeutic agents. Chemotherapeutic agents used in this method of treatment are melphalan, thiotepa (response rate, 50% to 60%), mechlorethamine, one of the above agents along with tumor necrosis factor and interferons (response rate, 91%).

Isolated limb perfusion

**Indications for Isolated Limb Perfusion:**

- Adjuvant to lymph node dissection
- Recurrent melanoma of extremity
- Bulky symptomatic melanoma of the extremity, with bleeding, ulceration, or edema.

**Role of radiation therapy for melanoma treatment in the adjuvant setting:**

Although melanoma is generally considered as a radioresistant tumor, radiation therapy has been found to be of clinical benefit after surgical lymph node resection in the following instances:

Multiple large lymph nodes, Extracapsular spread, Local recurrence in a previously dissected lymph node basin, Brain metastasis of melanoma.

It is relatively contraindicated in patients with xeroderma pigmentosa, epidermodysplasia verruciformis, or the basal cell nevus syndrome because RT may induce more tumors in the treated field. RT may have adjuvant use for unusually aggressive SCC and is used with or without surgery when metastasis involves regional lymph glands.

**Biologic Agents in Malignant Melanoma**

Interferon is used in metastatic setting, on the basis of its antiproliferative as well as immunomodulatory effects.
• The response rate in metastatic melanoma was approximately 16%.
• One third of these responses were complete responses.
• Responses could be observed up to 6 months after the therapy was initiated.
• Up to one third of the responses were durable.
• Patients with frequent interruptions due to side effects of interferon therapy did less well than those patients without interruptions.
• Patients with small-volume tumors did better than those with large-volume tumors.

**Interferon in the Adjuvant Setting in Malignant Melanoma**

Principle: There is a high incidence of relapse among patients with stage III melanoma after therapeutic or elective lymph node dissection and in those with thick melanoma lesions (>4 mm). The effect of interferon on disease-free survival has been evaluated in this setting. Melanoma vaccines are a type of specific active immunotherapy based on melanoma cell expression of certain HLA- and tumor-associated antigens. Vaccine types include whole cell preparations, cell lysates, gangliosides, peptides/proteins, dendritic cell vaccines, and DNA vaccines.

**Role of Chemotherapy in Melanoma:**

Melanoma is refractory to most cytotoxic agents. Objective response rates to single-agent chemotherapy are in the range of 10-23% and are typically of brief duration. Response rates to combination chemotherapy are somewhat higher but toxicity is increased with the use of multiple agents, and no survival advantage has been demonstrated. Dacarbazine (DTIC) has been considered a “standard” treatment, and temozolamide (Temodar), an oral methylating agent, is commonly used. In randomized trial comparing these agents, response rates were similar (13.5% with temozolamide and 12.1% with DTIC). Progression-free survival was slightly longer in the temozolamide arm (1.9 months vs 1.5 months), but there was no statistical difference in overall survival (7.7 and 6.4 months).6

Several lines of evidence suggest that melanoma is immunogenic. Lymphocytic infiltration and regression of primary cutaneous melanoma is common. Melanoma antigens with capacity to induce host T-cell responses have been identified and cloned. Interleukin-2 (IL-2)
is a central regulator of the cellular immune response, inducing activation and proliferation T-cells and NK-cells.

**Photodynamic therapy** (PDT) has been used to treat AKs by topically applying a photosensitizing porphyring or aminolevulinic acid (ALA) and then exposing the area to light. This process produces free radical oxygen species, which in turn cause tumor cell death. It has demonstrated effectiveness in less invasive BCCs and SCCs with a high cure rate in several studies. PDT is limited by the size of the lesion and significant photosensitizing after therapy. This therapy is still being evaluated for its future role in the treatment of skin cancers.6

Classic KS is at least initially—largely restricted to the surface of the body, and surgical resection is usually adequate for an excellent prognosis. In the case of disease that has spread (metastasized), further surgical procedures or chemotherapy may be required. Radiation can be used for multiple lesions in a restricted area, and chemotherapy yields satisfactory results for more disseminated disease. Lymphadenopathic KS can also be treated with chemotherapy or radiation therapy with good results. In immunosuppression-associated KS, withdrawal of immunosuppression (perhaps with adjunct chemotherapy or radiation therapy) is often effective. For AIDS-associated KS, antiretroviral therapy for HIV is usually helpful, with or without therapy targeted to the KS lesions. IFN-α and angiogenesis inhibitors are variably effective, while newer strategies aimed at specific intracellular kinase pathways or the downstream mammalian target of rapamycin are showing promise.73,74

**Immunotherapy:** Imiquimod, which is currently FDA approved for the treatment of superficial basal cell carcinoma and actinic keratoses,75

Newer noninvasive options for NMSC include topical chemotherapeutics, biological-immune-response modifiers, retinoids, and photodynamic therapy, which can be used particularly in patients with superficial tumors.76

**Palliative Care** The purpose of palliative care is to relieve symptoms and improve a patient’s quality of life, not cure the cancer. Patients with all stages of cancer may receive palliative
care. For example, a medication used to control nausea during chemotherapy is a form of palliative care because it is treating a symptom not the cancer.75

OUTCOME OF TREATMENT

A diagnosis of recurrent cutaneous SCC alone confers a more aggressive tumor subtype.77 Recurrent advanced stage cutaneous SCC confers a poor prognosis with an increased risk for parotid involvement, nodal metastasis, and poor locoregional control. Despite aggressive surgical resection including parotidectomy and neck dissection followed by postoperative radiotherapy, 5-year disease-free survival rates are less than 50%.78

In a study by Veness et al., improved locoregional control and disease-free survival (73% versus 54%, ) were achieved in patients who received adjuvant radiotherapy compared to surgery alone.79 In another series, 5-year disease-free survival was significantly improved for patients undergoing adjuvant radiotherapy following surgical resection (73% versus 18%, ), and locoregional control was maintained in 77% of patients.79

Distant metastasis noted in the immediate postoperative period was associated with poor prognosis. Median time to cancer recurrence was 6.5 months, and overall 2-year disease-free survival was 62%. Multiple studies have demonstrated that patients with parotid involvement are at a high risk for cervical metastasis77,80.

Patients with metastatic melanoma generally have a poor prognosis; survival is limited and typically measured in months rather than years. In general, the duration of survival is less than a year, a median of nearly 6 to 8 months. The 1-year survival rate is 45%, and less than 10% will live for 5 years or more. Multivariate analyses of prognostic factors have identified several independent factors that predict survival in this poor prognosis group, including the site of the first metastases, number of metastatic sites, and duration of remission.81

In the 2002 AJCC melanoma database analysis, the greatest difference in survival was found showing that patients with locoregional, distant nodal, and soft tissue metastasis have a better survival rate than the patients with visceral metastasis 6. Additionally, patients in whom the
lung was the only site of visceral metastasis had a better 1-year survival duration time compared with those with metastasis in other visceral sites. In the recent analysis of the AJCC melanoma database, separation of patients into three groups based on sites of disease produced the greatest splay in median survival.

Patients with melanoma metastasis to visceral sites other than the lung had a median survival of 7 months, those with lung metastases had a median survival of 12 months, and those with metastasis to nonvisceral sites (i.e., skin, subcutaneous tissue, and distant lymph nodes) had a median survival of 18 months. In general, patients who have visceral metastases to sites other than the lung, such as the liver, brain, or bone, do poorly with a median survival ranging from 3 to 6 months. Patients with one distant metastatic site have a significantly improved outcome compared with those with two or more distant sites.

Tas in a study reported that the initial sites of distant metastases are most commonly the skin, subcutaneous tissue, and lymph nodes, which occurred in 42% to 59% of patients in various studies. Visceral metastases were the initial sites of relapse in approximately 25% of all metastatic melanoma patients. The most common sites of visceral metastases were the lung (18–36%), brain (12–20%), liver (14–20%), and bone (11–17%). In conclusion, lifetime follow-up of melanoma patients, particularly during the first three years, is necessary because the expected cure is rarely achieved after surgical excision and also given adjuvant treatment. The fact that over half of all recurrences/metastases occurred within 3 years urges us to concentrate follow-up in the early time periods following diagnosis. Generally, the prognosis of patients with metastatic melanoma is poor; however, because the clinical behavior of metastatic melanoma is variable, significant factors for survival consisting of site of metastasis and number of metastatic sites should be emphasized.

Brien noted in multivariate analysis that factors found to have an independent effect on survival were immunosuppression, advanced clinical parotid stage (P3), and pathologic neck node involvement. Survival also varied significantly with P stage, with 2-year survival of 88%, 62%, and 30% for stages P1, P2, and P3, respectively. Immunosuppressed patients had a significantly worse survival rate than those who were not immunosuppressed. Also, Patients treated with radiotherapy alone had a significantly worse outcome than those treated with surgery alone or combined surgery and radiotherapy. Patients pathologically staged N1
and N2 had identical 5-year survival of approximately 60%, significantly worse than the 80% in patients who had neck dissections but were found to have an absence of nodal involvement.

**Prevention of skin cancer**

Exposure to ultraviolet solar radiation, especially ultraviolet B (UVB; 290 to 320 nm), is the most common cause of skin cancer and the most preventable.\(^5\)

*Primary prevention* of melanoma involves the avoidance of sun and other reducible risk factors. Patients should be educated about the risk factors for developing melanoma ultraviolet light. Use of sunblock and light clothing should be encouraged. Patients should be educated about clinical features of melanoma and precursor lesions and should be taught to perform self-examination of the skin.\(^18\) Proper wound care, protective footwear and human immunodeficiency virus (HIV) control can substantially reduce the incidence, morbidity and mortality of skin cancer.

*Secondary prevention* depends on careful physical examination and biopsy of all suspicious skin lesions.\(^40\) Close surveillance is required in high-risk patients. Digital photographs are used for comparing the multiple pigmented skin lesions and for assessing any changes as described previously.\(^18\)

**Prognosis**

The major prognostic determinant of these deadly neoplasms is the depth of invasion. Melanomas >3.65mm thick have poor prognosis as 60% will develop metastases and die from the disease. Unfortunately due to late presentation all our cases were nodular melanomas more than 1.0cm thick in contrast to Melanomas in White people which are predominantly non-invasive - superficial spreading or lentigo maligna. Thus although melanomas are commoner in Whites the prognosis is poorer in Blacks.\(^8\)

Recurrence risk factors for SCC include tumor size and location, poor border definition, recurrent tumor, immunosuppression, and site of prior radiation. Additional risk factors include site of a chronic inflammatory process; rapid tumor growth; neurologic symptoms;
moderate-to-poorly differentiated adenoid, adenosquamous (with mucin production), or desmoplastic histology; Clark level IV to V (deep reticular dermis to subcutaneous fat) or thickness of 4 mm; and perineural or vascular invasion.\textsuperscript{5} BCC recurrence is after treatment influenced by aggressive histology (morpheaform, sclerosing, infiltrative, micronodular), multifocality, and perineural involvement. The majority of recurrences occur within 3 years of treatment, and metastases are rare.\textsuperscript{85}

The prognostic factors of melanoma include.\textsuperscript{18}

<table>
<thead>
<tr>
<th>Good prognostic factors</th>
<th>Poor prognostic factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Tumor involving an extremity</td>
<td>Melanoma of the skin of the trunk, head, and neck</td>
</tr>
<tr>
<td>2. Thin tumor</td>
<td>Thick tumor</td>
</tr>
<tr>
<td>3. No ulceration of tumor</td>
<td>Tumor ulceration present</td>
</tr>
<tr>
<td>4. Radial growth pattern</td>
<td>Nodular histology</td>
</tr>
<tr>
<td>5. Early stage (stage I and II)</td>
<td>Late stage at presentation (stage III and IV)</td>
</tr>
<tr>
<td>6. Absence of vascular and/or lymphatic invasion</td>
<td>Presence of vascular and/or lymphatic invasion</td>
</tr>
<tr>
<td>7. Low tumor cell mitotic rate</td>
<td>High tumor cell mitotic rate</td>
</tr>
</tbody>
</table>

Women have a better prognosis than do men when matched by age and stage of disease.\textsuperscript{40}

MATERIALS AND METHODS
Study Area

The study was carried out in the Radiotherapy department, University College Hospital, Ibadan, Oyo state, Nigeria

Study population,

Skin cancer treated at the radiotherapy department between January 2001 and December 2010.

Inclusion criteria

Histologically diagnosed primary skin cancer

Exclusion criteria

1. Skin cancer cases without histological diagnosis.
2. Secondary metastases to the skin sites.
3. Tumors not classified under skin cancer

Study design

This is a retrospective study.

Data collection

All available radiotherapy treatment records and case files of skin cancer cases attended to between January 2001 and December 2010 were retrieved for data collection.

Data extracted included biodata, level of education, employment status and the duration of the illness. Pathological features like site of the disease, the stage at presentation, the lymph node status, the histological cell type and histological grade of the disease.

The site(s) of metastasis at presentation was determined from records of clinical examination and radiological tests during pretreatment evaluation. The treatment received for example, conservative or radical surgery, the chemotherapy regimen and number of cycles received, the site of radiotherapy treatment, the dose of radiotherapy treatment. The Outcome
of treatment was determined in terms of absence or presence of distant metastasis and the disease free interval as well as locoregional recurrence after treatment. The end point of observation or follow up was distant metastases within a period of two years.

**Data management**

The data obtained was analyzed using the Statistical Package for Social Sciences (SSPS) version 16.0 to determine the outcome of skin cancer treatment in Radiotherapy Clinic UCH, Ibadan.

**Ethical Considerations**

Ethical clearance to conduct the study was sought from the Joint Ethical Review Committee of the University of Ibadan/University College Hospital, Ibadan.

1. **Confidentiality of data:** Hospital numbers and not names of patients were used to maintain confidentiality. The record of patients were kept confidential and no third party had access to them. The data extraction forms was kept in a secured place, entered on the computer with the password protected and made accessible to the researcher only.

2. **Beneficence to patients:** The study is of benefit as its findings will be communicated to the stakeholders involved in providing care and support services to skin cancer patients.

**RESULTS:**
A total of one hundred and twenty six (126) cases with histologically diagnosed skin cancer were seen and analysed in this study within the study period. An average of 14.6 cases were seen per year. The highest number were recorded in 2008 and 2009 respectively (Figure 1). The age range of patient was 7 years to 98 years with mean age of 46.6 ±3.4.9 (Figure 2). The male to female ratio is 1.5:1. Most patients were farmers and secondary education was the highest educational status. A higher proportion of 44 (34.9%) patients were from the Southwest region followed by the Southeast 36 (28.5%) (Table 1). Trauma was identified as the most common predisposing factor consisting of 23 (18.3%) followed by albinism 20 (15.9%) and chemical exposures 19 (15%) as second and third common factors respectively (Table 2).

Squamous cell carcinoma had the highest proportion 63 (50%) followed by melanoma 30 (23.8%) while the least proportions 3 (2.4%) of histology types were found in adnexal tumour and Dermatofibrosarcoma (Table 3).

A higher proportion 45 (35.7%) of the patients seen had well differentiated, followed by undifferentiated 39 (30.9%). (Figure 3) The most common anatomical site affected was the lower limb with proportion of (59.5%) of followed by head and neck (22%), the least affected anatomical site was found in the thorax and abdomen (3%). (Figure 4)

Most patients had painless swelling, as the commonest presenting complaints and was observed in 51 (40.5%) while the least number of patients 3 (2.4%) had numbness as their presenting symptoms (Table 4). A higher number of patient presented with stage 3 followed by stage 4 disease (Table 5). Lung was the commonest site of distant metastases as seen 50% of patients in stage IV disease followed by liver 20% (Table 6)

Patients with Basal cell carcinoma had a higher proportion of 13 (61.9%) patients with symptom free interval of 2 years compared to other histology types (Table 7). Lungs had the highest site of distant metastasis 11 (50%), followed by liver 4 (20%) while brain had least metastasis (8)
Stage IV disease had the highest proportion 12 (57.1%) of distant metastasis. No distance metastasis was observed in stage I and II (Table 9). Most patients had excision surgery for diagnostic and therapeutic purpose, only 4% of the patients had amputation for recurrent and late stage diseases. Radiotherapy dose of 40-49 Gy was received by most patients 63.9%, the commonest site effect was erytherma (37%). Cisplatin and 5-fluorouracil regime was received by 54.5% of patients with nausea and vomiting as the commonest site effect. Malignant melanoma had the highest distance metastasis 6 (20.0%) while squamous cell carcinoma had the highest locoregional 30 (47.6%). Residual disease was observed more patients with Kaposi sarcoma and Dermatofibrosarcoma (Table 10).

Patients with early stage have 86.8% tendency of survival compared to those in the late stage of 86.3%. Though, the difference in the survivorship is not statistically significant with p-value>0.05 (Table 11).

Patients that received surgery and radiotherapy has the highest survival rate of 88.2% while chemotherapy showed the least survivorship rate of 83.3%. With p-value 0.012(<0.05), it is clearly evident that the various treatment outcomes is statistically significant. (Table 12)

At the end of the study, a higher proportion 69 (59.0%) of male patient were lost to follow up, while equal proportions (50%) male and female patients were dead and a higher proportion 12 (80.0%) of male patients were alive at the end of the study.
Figure 1: Annual Frequency of Skin Cancer

The age range of the patients was 7 to 98 years with mean age of 46.6 years. The peak age group was 40-49 years accounting for 22.2% of the patients.
<table>
<thead>
<tr>
<th>Gender</th>
<th>Frequency</th>
<th>Percentage(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>77</td>
<td>61.1</td>
</tr>
<tr>
<td>Female</td>
<td>49</td>
<td>38.9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Frequency</th>
<th>Percentage(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Civil servant</td>
<td>27</td>
<td>21.4</td>
</tr>
<tr>
<td>Student</td>
<td>3</td>
<td>2.4</td>
</tr>
<tr>
<td>Private worker</td>
<td>12</td>
<td>9.5</td>
</tr>
<tr>
<td>Unemployed</td>
<td>24</td>
<td>19</td>
</tr>
<tr>
<td>Farming</td>
<td>57</td>
<td>45.2</td>
</tr>
<tr>
<td>Trader</td>
<td>3</td>
<td>2.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Geographical Location</th>
<th>Frequency</th>
<th>Percentage(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>South west</td>
<td>44</td>
<td>34.9</td>
</tr>
<tr>
<td>South east</td>
<td>36</td>
<td>28.5</td>
</tr>
<tr>
<td>South south</td>
<td>30</td>
<td>23.8</td>
</tr>
<tr>
<td>North central</td>
<td>9</td>
<td>7.2</td>
</tr>
<tr>
<td>North west</td>
<td>4</td>
<td>3.2</td>
</tr>
<tr>
<td>North East</td>
<td>3</td>
<td>2.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Education</th>
<th>Frequency</th>
<th>Percentage(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary education</td>
<td>30</td>
<td>23.8</td>
</tr>
<tr>
<td>Secondary education</td>
<td>54</td>
<td>42.9</td>
</tr>
<tr>
<td>Tertiary education</td>
<td>39</td>
<td>31</td>
</tr>
<tr>
<td>No formal education</td>
<td>3</td>
<td>2.4</td>
</tr>
</tbody>
</table>

A higher proportion 77(61.1%) of patients was male compared to female 49(38.9%). 57(45.2%) of the patients were farmers followed by civil servants 27(21.4%) and the least proportion 3(2.4%) were found in students and traders respectively. A higher proportion 44(34.9%) of the patients was from south west and the least was from north east 3(2.4%). A greater proportion 54(42.9%) of the patients had secondary school education.
Table 2- Distribution Table of Pre-disposing Factors

<table>
<thead>
<tr>
<th>PRE-DISPOSING FACTORS</th>
<th>FREQUENCY</th>
<th>PERCENTAGES (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trauma</td>
<td>23</td>
<td>18.3</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>12</td>
<td>9.5</td>
</tr>
<tr>
<td>Alcohol</td>
<td>14</td>
<td>11.1</td>
</tr>
<tr>
<td>Albinism</td>
<td>20</td>
<td>15.9</td>
</tr>
<tr>
<td>Chemical exposures</td>
<td>19</td>
<td>15</td>
</tr>
<tr>
<td>Ionizing Radiation</td>
<td>6</td>
<td>4.8</td>
</tr>
<tr>
<td>Prolonged Sun exposure</td>
<td>9</td>
<td>7.1</td>
</tr>
<tr>
<td>Family history</td>
<td>6</td>
<td>4.8</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>4</td>
<td>3.2</td>
</tr>
<tr>
<td>Melanocytic naevi</td>
<td>3</td>
<td>2.4</td>
</tr>
<tr>
<td>Unspecified</td>
<td>10</td>
<td>7.9</td>
</tr>
</tbody>
</table>

Trauma had the highest proportion 23(18.3%) as the pre-disposing factor, followed by albinism 20 (15.9%) while melanocytic naevi had the least in frequency 3(2.4%).

Table 3-Histology Types

<table>
<thead>
<tr>
<th>Histology</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal cell carcinoma</td>
<td>21</td>
<td>16.7%</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>63</td>
<td>50%</td>
</tr>
<tr>
<td>Melanoma</td>
<td>30</td>
<td>23.8%</td>
</tr>
<tr>
<td>Kaposi sarcoma</td>
<td>6</td>
<td>4.8%</td>
</tr>
<tr>
<td>Mycoses fungoides</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Merkel cell tumors</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Adnexal tumour</td>
<td>3</td>
<td>2.4%</td>
</tr>
<tr>
<td>Dermatofibrosarcoma</td>
<td>3</td>
<td>2.4%</td>
</tr>
<tr>
<td>Total</td>
<td>126</td>
<td>100%</td>
</tr>
</tbody>
</table>

Squamous cell carcinoma had the highest proportion 63 (50%) while the least proportions 3(2.4%) of histology types were found in adnexal tumour and Dermatofibrosarcoma.
A higher proportion 45(35.7%) of the patients seen had well differentiated, followed by undifferentiated 39(30.9%).

![Pie chart showing histological grade distribution](image)
A higher proportion (59.5%) of the anatomical site affected was found in the lower limb, followed by head and neck (22%), the least affected anatomical site was found in the thorax and abdomen (3%).

Table 4 - Symptoms distribution

<table>
<thead>
<tr>
<th>symptoms</th>
<th>Frequency</th>
<th>Percentage(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>24</td>
<td>19</td>
</tr>
<tr>
<td>Painful Swelling</td>
<td>27</td>
<td>21.4</td>
</tr>
<tr>
<td>Numbness</td>
<td>3</td>
<td>2.4</td>
</tr>
<tr>
<td>Ulceration</td>
<td>12</td>
<td>9.5</td>
</tr>
<tr>
<td>Skin discoloration</td>
<td>9</td>
<td>7.1</td>
</tr>
<tr>
<td>Painless swelling</td>
<td>51</td>
<td>40.5</td>
</tr>
<tr>
<td>Total</td>
<td>126</td>
<td>100</td>
</tr>
</tbody>
</table>

A higher proportion 51(40.5%) of patients had painless swelling, while the least proportion 3(2.4%) had numbness as their presenting symptoms.
A higher proportion 55(43.7\%) of the patients presented with Stage 3, followed by stage 4 28(22.2\%) and the least 18(14.3\%) was in stage 1.

<table>
<thead>
<tr>
<th>Stage at presentation</th>
<th>Frequency</th>
<th>Percentage(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>18</td>
<td>14.3</td>
</tr>
<tr>
<td>Stage 2</td>
<td>25</td>
<td>19.8</td>
</tr>
<tr>
<td>Stage 3</td>
<td>55</td>
<td>43.7</td>
</tr>
<tr>
<td>Stage 4</td>
<td>28</td>
<td>22.2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>126</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>
Table 6-Distant Metastasis of Skin Cancer (stage IV) at presentation

<table>
<thead>
<tr>
<th>Site of metastasis</th>
<th>frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lungs</td>
<td>11</td>
<td>50%</td>
</tr>
<tr>
<td>bone</td>
<td>2</td>
<td>10%</td>
</tr>
<tr>
<td>Liver</td>
<td>4</td>
<td>20%</td>
</tr>
<tr>
<td>Brain</td>
<td>1</td>
<td>5%</td>
</tr>
<tr>
<td>Subcutaneous area</td>
<td>3</td>
<td>15%</td>
</tr>
</tbody>
</table>

Lungs had the highest site of distant metastasis 11(50%) , followed by liver 4(20%) while brain had least metastasis 1(5%).

Table 7- Association between symptom free interval(SFI) and histology of the tumour

<table>
<thead>
<tr>
<th>Histology</th>
<th>SFI 1yr or less</th>
<th>SFI 2yr</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal cell carcinoma</td>
<td>17(81.0%)</td>
<td>13 (61.9%)</td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>39(61.9%)</td>
<td>23(36.5%)</td>
<td></td>
</tr>
<tr>
<td>Melanoma</td>
<td>11(36.7%)</td>
<td>8(26.7%)</td>
<td></td>
</tr>
<tr>
<td>Kaposi Sarcoma</td>
<td>3(50.0%)</td>
<td>2(33.4%)</td>
<td>0.62</td>
</tr>
<tr>
<td>Dermatofibrosarcoma protuberance</td>
<td>2(66.7%)</td>
<td>0(0.0%)</td>
<td></td>
</tr>
<tr>
<td>Adnexal tumour</td>
<td>1(33.3%)</td>
<td>1(33.3%)</td>
<td></td>
</tr>
</tbody>
</table>

Patients with Basal cell carcinoma histology types had a higher proportion 17(81.0%) with SFI less than or equal to 1year and 2year SFI 13(61.9%) compared to proportion of patients 1 (33.3%) with adnexal tumours of less than 1 year and 2years. This association is not statistically significant (p=0.62).
Table 8-Distant Metastasis of Skin Cancer (stage IV) at presentation and two-years follow up

<table>
<thead>
<tr>
<th>Site of metastasis</th>
<th>Frequency(%) at presentation</th>
<th>Frequency(%) at 2 years follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lungs</td>
<td>11(50.0%)</td>
<td>3(37.5%)</td>
</tr>
<tr>
<td>bone</td>
<td>2(10.0%)</td>
<td>1(12.5%)</td>
</tr>
<tr>
<td>Liver</td>
<td>4(20.0%)</td>
<td>2(25.0%)</td>
</tr>
<tr>
<td>Brain</td>
<td>1(5.0%)</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>Sub cutaneous area</td>
<td>3(15.0%)</td>
<td>1(12.5%)</td>
</tr>
</tbody>
</table>

Lungs had the highest site of distant metastasis 11(50%) , followed by liver 4(20%) while brain had least metastasis 1(5%)

Table 9- Stage and One year treatment outcome

<table>
<thead>
<tr>
<th>Stage</th>
<th>Outcome of treatment</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Locoregional recurrence</td>
<td>Distant metastasis</td>
</tr>
<tr>
<td>Stage 1</td>
<td>9(50.0%)</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>Stage 2</td>
<td>15(55.6%)</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>Stage 3</td>
<td>27(56.2%)</td>
<td>6(12.5%)</td>
</tr>
<tr>
<td>Stage 4</td>
<td>6(28.6%)</td>
<td>12(57.1%)</td>
</tr>
</tbody>
</table>

Stage 4 had the highest proportion 12 (57.1%) of distant metastasis , No distance metastasis was observed in stage I and II. Stage 1 had 2 years SFI of 50%. This association is statistically significant (p<0.05).
Table 10- Histology types and One year treatment outcome

<table>
<thead>
<tr>
<th>Stage</th>
<th>Outcome of treatment</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Locoregional recurrence</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Distant metastasis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Residual</td>
<td></td>
</tr>
<tr>
<td>Basal cell carcinoma</td>
<td>3(14.3%)</td>
<td>3(14.3%)</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>30(47.6%)</td>
<td>9(14.3%)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>12(40.0%)</td>
<td>6(20.0%)</td>
</tr>
<tr>
<td>Kaposi sarcoma</td>
<td>2(33.3%)</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>Dermatofibrosarcoma</td>
<td>1(33.3%)</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>Adnexal tumour</td>
<td>3(100.0%)</td>
<td>0(0.0%)</td>
</tr>
</tbody>
</table>

Basal cell carcinoma had the highest proportion 15(71.4%) of 2 years SFI. Malignant melanoma had the highest distance metastasis 6(20.0%) while squamous cell carcinoma had the highest locoregional 30 (47.6%). Kaposi sarcoma and Dermatofibrosarcoma had the highest proportion of residual disease.

Table 11 Summary statistics for survivorship between early stage and late stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>Probability for survival</th>
<th>Median survival</th>
<th>Standard error</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early</td>
<td>0.868</td>
<td>6</td>
<td>0.047</td>
<td>0.7</td>
</tr>
<tr>
<td>Late</td>
<td>0.863</td>
<td>4</td>
<td>0.040</td>
<td></td>
</tr>
</tbody>
</table>

Patients with early stage have 86.8% tendency of survival compared to those in the late stage of 86.3%. Though, the difference in the survivorship is not statistically significant with p-value>0.05
Figure: 5

Survival Functions

Cum Survival

Stage in 2 groups
- Early stage
- Late stage
- Early stage-censored
- Late stage-censored

Time in years
Table 12: Summary: Survivorship for Treatments received

<table>
<thead>
<tr>
<th>Treatment received</th>
<th>Probability for survival</th>
<th>Median survival</th>
<th>Standard error</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery and radiotherapy</td>
<td>0.882</td>
<td>6</td>
<td>1.998</td>
<td>0.012</td>
</tr>
<tr>
<td>Surgery, radiotherapy &amp; chemotherapy</td>
<td>0.868</td>
<td>4</td>
<td>0.798</td>
<td></td>
</tr>
<tr>
<td>Radiotherapy and chemotherapy</td>
<td>0.818</td>
<td>3</td>
<td>0.425</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>0.833</td>
<td>2</td>
<td>0.742</td>
<td></td>
</tr>
</tbody>
</table>

Patients that received surgery and radiotherapy has the highest survival rate of 88.2% while chemotherapy showed the least survivorship rate of 83.3%. With p-value 0.012(<0.05), it is clearly evident that the various treatment outcomes is statistically significant.
At the end of the study, a higher proportion 69(59.0%) of male patients were lost to follow up, while equal proportions (50%) of male and female patients were dead and a higher proportion 12(80.0%) of male patients were alive at the end of the study.

<table>
<thead>
<tr>
<th>End of Study</th>
<th>Male(%)</th>
<th>Female(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss to follow up</td>
<td>69(59.0%)</td>
<td>43(41.0%)</td>
</tr>
<tr>
<td>Dead</td>
<td>3(50.0%)</td>
<td>3(50.0%)</td>
</tr>
<tr>
<td>Alive</td>
<td>12(80.0%)</td>
<td>3(20.0%)</td>
</tr>
</tbody>
</table>
DISCUSSION

There was increase in incidence of skin cancer as observed in this study with an average of 14.6 cases seen per year and highest number of cases (25) being recorded in 2008 and 2009 respectively. This study concurred with the report of Asuquo et al 2011 which showed an average of 15.2 cases in a ten-year skin cancer review in Calabar, South-south, Nigeria.

There is increasing incidence of skin cancer worldwide because of increase in exposure to ultra-violet light and ozone layer depletion due to increased environmental and industrial pollution. Immunosuppression may be another factor as patients with immunosuppression are more prone to develop non-melanoma skin cancers.

Skin cancer occurred more in middle aged adult with a mean age of 46.6 years. This is in line with report of another study in Nigeria by Asuquo et al 2011 who found that the mean age of skin cancer patients was 43 yrs. The Peak age of incidence varies with the type of cancer, genetic predisposing and ultraviolet light exposure.

Opara et al 2010 in eastern Nigeria reported that 61% of skin cancer patients in albino were below 40 years while Onunu et al 2007 in Benin reported that the Kaposi sarcoma patients with HIV seropositivity had a mean age of 36.3 years. In another study by Samaila et al in Zaria, it was reported that peak age of incidence of melanoma was fifth and sixth decades while Ochicha etal in Kano noted that malignant skin tumours most frequently occurred in the sixth and seventh decades.

Gender distribution showed male to female ratio of 1.6:1 indicating male predominance in this study. This agrees with previous studies in Nigeria. The increased male gender could be attributed to males being more exposed to sunlight because of their outdoor operations. However, some other local and international studies showed equal male to female distribution.
Other socio demographic patterns observed in this study included higher number among patient with secondary school education, higher number among farmer, and higher number in patients from the South- western region. These may be a reflection of the overall demographic profile of the Western part of Nigeria .

The highest proportion of patients had trauma as the predisposing factor, followed by albinism and chemical exposure as the second and third predisposing factors respectively. Trauma as the major risk factor in this study is in agreement with other studies in this environment. 

Mandong et al 2000 in Jos reported that while sun exposures is the major aetiological factor in whites, chronic ulcers and inflammation appear to be the leading risk factor in Blacks. Sun exposure may not be the major risk factor in black because of the high level of melanin protection against effect of ultra violet rays from the sun. Another study in Nigeria reported that albinism appeared to be the most important risk factor in the development of skin cancer.

Squamous cell carcinoma (SCC) had the highest frequency of the histology subtypes, followed by melanoma, Basal cell carcinoma (BCC) and Kaposi sarcoma(KS) as the second, third and fourth histology subtype . SCC as the most common histology in this study is in line with other Nigerian studies and this is in contrast to the findings in caucasians. Solan et al reprecated that BCC accounted for 80% while SCC accounted for 20% of NMSC. SCC is also the commonest cutaneous malignancies among the albinos.

SCC and KS are both related to immunosupression . SCC as the commonest histology subtype could also be related to immunosuppression which could be a predisposing factor. KS was noted to be rising in this region due to increased prevalence of HIV infection.

Melanoma is the second highest malignancy in this study. This in line with another study in Nigeria. The incidence rates of melanoma showed substantial worldwide variation. The highest incidence of
malignant melanoma are in Australia, Auckland, New Zealand and the lowest incidence are reported in Asian population in China, Japan and Singapore.\textsuperscript{1,3,19}

Black Africans and Asians, twenty percent of the world’s melanoma.\textsuperscript{100} Apart from sunlight other predisposing factors include pre-existing naevus, some genetically determined diseases such as xeroderma pigmentosa and von recklinghausen’s disease as well as exposure to chemical carcinogens.

In Nigeria, melanoma appears to be arising from existing epidermal melanocytes (de novo) and not from pre-existing naevus cell.\textsuperscript{96} An important feature of melanoma is that it is rare in dark skinned individual than the light skinned patients.

In overall the commonest presenting complaint in this study was painless swelling. However, symptoms vary with the histology subtypes. Patients with SCC had more swelling, while melanoma patients had more of skin discoloration. The most common affected anatomical site in this study was the lower limb and gluteal region, followed by head and neck region. This is in line with previous Nigerian studies.\textsuperscript{7,11} This could be due increased risk of trauma to the lower limb.

The highest proportion of patients presented with stage III disease, followed by stage IV. This agrees with the study by Yakubu et al 1995 who reported that skin cancer patients usually presented late with advanced fungating lesions beyond curative surgery.\textsuperscript{101} Lymphatic nodal involvement were higher with the ipsilateral inguinal node region having the highest proportion. This is line with previous studies by Tas 2012 who reported that initial sites of distant metastasis are most commonly the skin, subcutaneous tissue and lymph nodes.\textsuperscript{4,81} Wagner et al also reported that the draining lymph nodes are frequently involved after vertical growth in skin cancer.\textsuperscript{46}

Lung had the commonest site of metastasis in this study, followed by liver and bone as the second and third sites of metastasis respectively. This is in agreement with study by Milligan et al 2007 who reported that lung, liver, bone and lately brain were the common sites of metastasis.\textsuperscript{103}
Most of the patients had excision surgery both for diagnostic and therapeutic purpose. Only 4% had amputation for late stage BCC or SCC. Simple Surgical treatments or radiation therapy offer equivalent excellent cure rates of 90% to 95%. However, treatment approach must be individualized based on specific risk factors and patient characteristics for the most acceptable cosmetic and functional outcome. Overall, surgery is preferred for most patients. Extensive surgery is however necessary for patients with deeply invasive tumours.

Most patients (85.0%) had external beam radiotherapy for both radical and palliative treatment, while radical treatment was for cure in patients with early stage disease, palliative treatment was for pain control, imminent fracture and securing haemostasis. Post operative (adjuvant) radiotherapy is indicated if there were presence of positive surgical margins, perineural spread, invasion of bones and cartilage lymph node metastasis and extensive skeletal muscles infiltration. Radiotherapy reduces local recurrence rate in both melanoma and NMSC.

A higher proportion of patients in this study had radiotherapy of dose range 40-49Gy with the commonest side effect being erythema which was seen in (37.1%) of the patients. These patients were treated with cobalt 60 machine. 75.6% had chemotherapy which was indicated for metastatic disease.

The most commonly administered chemotherapy in this study was cisplatin and 5-fluorouracil regimen. This was received by 54.5% of patients given over 5-6 courses with nausea and vomiting being the commonest side effect.

Excellent response rates have been reported for advanced cases of SCC and BCC treated with cisplatin in combination with 5-fluorouracil.

In the outcome of treatment, a higher proportion of patients with basal cell carcinoma had higher symptom free interval in the first year and second year of follow up respectively while the patients
with dermatofibrosarcoma protuberance had no symptom free interval. Also, there were reduction in
distance metastasis following treatment compared to time of initial presentation as observed in stage
IV disease.

Patients with stage I and stage II disease at presentation had no distant metastases at 2 year post
treatment as compared to patient with stage III and IV disease. A higher proportion of patients with
melanoma in this study had distant metastases as compared to patients with other histology subtypes
who had either lower or no distant metastases indicating the propensity of high haematogeneous
spread by melanoma as well as the resistance to radiotherapy and chemotherapy.

Milligan et al reported on the increased locoregional control of melanoma by radiotherapy. Wagner et al also reported that about 5% of patients with melanoma present with symptoms of distant metastases without an apparent primary site.
CONCLUSION

This study highlighted that the common age of presentation of skin cancer was fifth decade with slight male predominance observed. Trauma was identified as the most common risk factor followed by albinism in skin cancer with SCC being the commonest histology. Lower limb was the most anatomically affected site followed by head and neck with painless swelling being the commonest presenting symptom.

The most common site of distant metastasis at both presentation and follow up was the lungs. Stage 3 was the commonest stage of presentation followed by stage 4.

Excision surgery is the main treatment modality in skin cancer. The radiotherapy dose range of 40-49 was received by most patients. Cisplatin and 5 fluorouracil was most frequently used, given over 5-6 courses with the commonest site effect being nausea and vomiting. Higher symptom free interval was noted in patients with early stage disease. Patients with melanoma had the highest proportion of distant metastasis post treatment.
RECOMMENDATION

Most patients present in advanced stage with associated significant morbidity and mortality, therefore more awareness of skin cancer should be created by the government and health care providers on the need for patients to present to specialist once symptoms persist for more than two weeks.

The General practitioners and other related health workers should endeavour to make early referrals to teaching hospitals especially in cases of skin cancer as early diagnosis increases the survival rate. Government should also provide more radiotherapy centers.
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Appendix 1

### WHO histological classification of keratinocytic skin tumours

<table>
<thead>
<tr>
<th>Keratinocytic tumours</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal cell carcinoma</td>
<td>8060/3</td>
</tr>
<tr>
<td>Superficial basal cell carcinoma</td>
<td>8061/3</td>
</tr>
<tr>
<td>Nodular (solid) basal cell carcinoma</td>
<td>8067/3</td>
</tr>
<tr>
<td>Micronodular basal cell carcinoma</td>
<td>8060/3</td>
</tr>
<tr>
<td>Infiltrating basal cell carcinoma</td>
<td>8069/3</td>
</tr>
<tr>
<td>Fibroepithelial basal cell carcinoma</td>
<td>8063/3</td>
</tr>
<tr>
<td>Basal cell carcinoma with adnexal differentiation</td>
<td>8068/3</td>
</tr>
<tr>
<td>Basaloid squamous carcinoma</td>
<td>8064/3</td>
</tr>
<tr>
<td>Keratotic basal cell carcinoma</td>
<td>8050/3</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>8070/3</td>
</tr>
<tr>
<td>Acantholytic squamous cell carcinoma</td>
<td>8075/3</td>
</tr>
<tr>
<td>Spindle-cell squamous cell carcinoma</td>
<td>8074/3</td>
</tr>
<tr>
<td>Verrucous squamous cell carcinoma</td>
<td>8051/3</td>
</tr>
<tr>
<td>Pseudovascular squamous cell carcinoma</td>
<td>8072/3</td>
</tr>
<tr>
<td>Adenosquamous carcinoma</td>
<td>8060/3</td>
</tr>
<tr>
<td>Bowen disease</td>
<td>8081/2</td>
</tr>
<tr>
<td>Bowenoid papulosis</td>
<td>8071/1</td>
</tr>
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</table>

### WHO histological classification of melanocytic tumours

<table>
<thead>
<tr>
<th>Malignant melanoma</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Superficial spreading melanoma</td>
<td>8720/3</td>
</tr>
<tr>
<td>Nodular melanoma</td>
<td>8721/3</td>
</tr>
<tr>
<td>Lentigo maligna</td>
<td>8742/2</td>
</tr>
<tr>
<td>Acral-lentiginous melanoma</td>
<td>8743/3</td>
</tr>
<tr>
<td>Desmoplastic melanoma</td>
<td>8745/3</td>
</tr>
<tr>
<td>Melanoma arising from blue naevus</td>
<td>8780/3</td>
</tr>
<tr>
<td>Melanoma arising in a giant congenital naevus</td>
<td>8761/3</td>
</tr>
<tr>
<td>Melanoma of childhood</td>
<td>8720/3</td>
</tr>
<tr>
<td>Naevus melanoma</td>
<td>8720/3</td>
</tr>
<tr>
<td>Persistent melanoma</td>
<td>8720/3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Benign melanocytic tumours</th>
<th>Code</th>
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</thead>
<tbody>
<tr>
<td>Congenital melanocytic naevi</td>
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</tr>
<tr>
<td>Superficial type</td>
<td>8761/0</td>
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<tr>
<td>Proliferative nodules in congenital melanocytic naevi</td>
<td>8762/1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Descriptions</th>
<th>Code</th>
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<tr>
<td>Actinic keratosis</td>
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</tr>
<tr>
<td>Acantholysis of keratosis</td>
<td></td>
</tr>
<tr>
<td>PUVA keratosis</td>
<td></td>
</tr>
<tr>
<td>Verruca vulgaris</td>
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</tr>
<tr>
<td>Verruca plantaris</td>
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<tr>
<td>Verruca plana</td>
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</tr>
<tr>
<td>Acanthomas</td>
<td></td>
</tr>
<tr>
<td>Epidermodysplastic acanthoma</td>
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</tr>
<tr>
<td>Warty dyskeratoma</td>
<td></td>
</tr>
<tr>
<td>Acantholytic acanthoma</td>
<td></td>
</tr>
<tr>
<td>Lentigo simplex</td>
<td></td>
</tr>
<tr>
<td>Seborrheic keratosis</td>
<td></td>
</tr>
<tr>
<td>Melanocanthoma</td>
<td></td>
</tr>
<tr>
<td>Clear cell acanthoma</td>
<td></td>
</tr>
<tr>
<td>Large cell acanthoma</td>
<td></td>
</tr>
<tr>
<td>Keratoacanthoma</td>
<td></td>
</tr>
<tr>
<td>Lichen planus-like keratosis</td>
<td></td>
</tr>
<tr>
<td>Dermal melanocytic lesions</td>
<td></td>
</tr>
<tr>
<td>Mongolian spot</td>
<td></td>
</tr>
<tr>
<td>Naevus of Ito and Ota</td>
<td></td>
</tr>
<tr>
<td>Blue naevus</td>
<td>8780/0</td>
</tr>
<tr>
<td>Cellular blue naevus</td>
<td>8780/0</td>
</tr>
<tr>
<td>Combined naevus</td>
<td>8727/0</td>
</tr>
<tr>
<td>Melanotic macules, simple lentigo and lentiginous naevus</td>
<td></td>
</tr>
<tr>
<td>Dysplastic naevus</td>
<td>8727/0</td>
</tr>
<tr>
<td>Site-specific naevi</td>
<td></td>
</tr>
<tr>
<td>Acral</td>
<td></td>
</tr>
<tr>
<td>Genital</td>
<td></td>
</tr>
<tr>
<td>Meyerson naevus</td>
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<tr>
<td>Persistent (recurrent) melanocytic naevus</td>
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</tr>
<tr>
<td>Spitz naevus</td>
<td>8770/0</td>
</tr>
<tr>
<td>Pigmented spindle cell naevus (Reed)</td>
<td>8770/0</td>
</tr>
<tr>
<td>Halo naevus</td>
<td>8723/0</td>
</tr>
</tbody>
</table>
# TNM classification of skin carcinomas

## TNM classification

### T - Primary tumour
- **TX**: Primary tumour cannot be assessed
- **T0**: No evidence of primary tumour
- **Tis**: Carcinoma in situ
- **T1**: Tumour 2 cm or less in greatest dimension
- **T2**: Tumour more than 2 cm but no more than 5 cm in greatest dimension
- **T3**: Tumour more than 5 cm in greatest dimension
- **T4**: Tumour invades deep extradermal structures, i.e., cartilage, skeletal muscle, or bone

Note: In the case of multiple simultaneous tumours, the tumour with the highest T category is classified and the number of separate tumours is indicated in parentheses, e.g., T2(s).

### N - Regional lymph nodes
- **NX**: Regional lymph nodes cannot be assessed
- **N0**: No regional lymph node metastasis
- **N1**: Regional lymph node metastasis

### M - Distant metastasis
- **MX**: Distant metastasis cannot be assessed
- **M0**: No distant metastasis
- **M1**: Distant metastasis

### Stage grouping

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>NO</td>
<td>M0</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>NO</td>
<td>M0</td>
</tr>
<tr>
<td>Stage II</td>
<td>T2, T3</td>
<td>NO</td>
<td>M0</td>
</tr>
<tr>
<td>Stage III</td>
<td>T4</td>
<td>NO</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>
APPENDIX 3

DATA EXTRACTION FORM

1. Serial No…………………………………………………………………………………………
2. Name (Initials Only)…………………………………………………………………………
3. Hospital No:……………………………………………………………………………………
4. Age(years):……………………………………………………………………………………
5. Sex: 1. Male 2. Female
6. Occupation:……………………………………………………………………………………
7. State of origin:………………………………………………………………………………
8. Source of Referral:…………………………………………………………………………
9. Marital Status
10. Level of Education
11. Social Habits: Smoking……. Alcohol……… Others………
12. Family History:
13. Presenting Compliant
    Pain……. Swelling……. Numbness……. Ulceration…….
    Bleeding…… Skin discoloration…… Loss of function…… Others…….
14. Duration of Illness before presentation: a)……… b) ……. c)………
15. Anatomical Site affected: Head and Neck……. Trunk……. Upper limbs…….
    Lower limb
16. Histology:……………………………………………………………………………………
17. Grade (Differentiation): Well:………. Moderate:………. Others:………
18. Date of Diagnosis:…………………………………………………………………………
19. Stage of primary disease at Presentation.
Stage:…… Early Locally/regionally Advanced…………… Recurrent…………
Metastastic……………

20. Metastatic site : Node involvement ; 1, level …… 2 single …… 3 matted……


21. Tissue/ Organ First Affected:……………………

22. Surgery1). Conservative Surgery 2.) Radical Surgery

23. Radiotherapy

   1. Site of Treatment………… 2. Dose…………

   3. Duration of Treatment


   If yes state regimen………… No of Cycles……

25. Targeted Therapy 1. Yes 2. No

   If yes specify………………

26. a) Other treatment received


27. Outcome of Treatment

   1. No locoregional recurrence or distant metastasis

   2. Locoregional recurrence alone (specify site(s))………………

   3. Locoregional recurrence and distance metastasis (specify site(s))………………

   4. Distant metastasis alone(specify site(s))……………………

   5. Progressive disease

28. Disease Free Interval

   1. Loco regional recurrence free interval…………………(in years)

   2. Distance metastasis free interval………………………..(in years).
3. Symptom free interval…………………………………………( in years)

29 End point of study ………….. ………………..(in years) post complete treatment

30 a) last chemotherapy date……. b) last Radiotherapy date

31 Co morbidities/ confounders ………..