Sudan University of Science and Technology

College of Graduate Studies

Study of the factors affects the five years survival rate of prostate cancer patient in Sudan

دراسة العوامل المؤثرة علي معدل البقاء علي قيد الحياة لخمس سنوات لمريض سرطان البروستاتا في السودان

A thesis Submitted for the Fulfillment of the Requirements for the Degree of PhD in nuclear medicine

By

Fahad Ahmed Mohammed Ali

(B.Sc. In Radiotherapy)

(M.Sc. In Nuclear Medicine)

Supervisor

Assoc. prof. **Mohammed Elfadil Mohammed**

2016

الآية

قال تعالى:

﴿وَاللَّهُ خَلَقَكُمْ ثُمَّ يَتَوَفَّاكُمْ وَمِنْكُمْ مَنْ يُرَدُّ إِلَى أَرْذَلِ الْعُمُرِ لِكَيْ لَا يَعْلَمَ بَعْدَ عِلْمٍ شَيْئًا إِنَّ اللَّهَ عَلِيمٌ قَدِيرٌ﴾

سورة النحل الاية (70)

Dedication:

To the soul of my father. He died from cancer

To my mother for her endless Love

To my wife for unlimited Support

And To my kids

Acknowledgement

After more than Three Years, today is the day for writing this note of thanks. First deeply grateful to God who gave me patience and power to complete my thesis; then to my supervisor, Dr. Mohammed Elfadil Mohammed - (associate professor) for his great support and valuable guidance. and also would like to express my special thanks of gratitude to my co- supervisor Dr. Yousif Abdullah, assistant Professor at Majmaah University; for their unlimited support and comments.

Abstract

Prostate cancer considers one of the furthermost tumors in world; it classify second among all cancers after breast cancer. It likewise the most common type among the Sudanese males. The five-year survival rate is the percentage of patients live five years after the disease is diagnosed used to evaluate the effectiveness of diagnosis and treatments. There are many methods to calculate the five-year survival rate in my thesis used direct method, observed, corrected and Relative survival rate. The aim of this study was to Study the factors affects the five year survival rate of prostate cancer in Sudan. This study was conducted in Sudan during the period from July 2013 to June 2016. One thousand, one hundred and seventy seven patients were included in the study; they were processed to determine the common age, Region, marital status, patient parents relative and incidence of all prostate cancer record in statistic office in RICK from January 2010 to December 2012. About three hundred and six patients were studied through 5 years in order to assess the status of survival. This study through direct method found that only 111 out of 306 (36.3%) patients were surviving 5 years after the date of first treatment. Estimation of the 5YSR of prostate cancer for patients age 45 to 97 years by observed, corrected and expected five survival of the population in respect to Kalban-Meier calculation methods , the study found that the survival rates were 39%, 42% and 44% ($p > 0.05$) respectively. This study found that there were many factors affected the survival rate in Sudan population such as age, treatment type, grade and site of metastases. In conclusion 5YSR can be estimated in Sudanese by using the following linear equation as indigenous formula: Survival rate = (-1.396 × Grade) + (0.19 × Treatment) + (-0.105 × Site of MITS) + 6.53.

المستخلص

سرطان البرستاتا من اكثر السرطانات انتشارا في العالم ويحتل المركز الثاني بعد سرطان الثدي ويعتبر من اكثر السرطانات عند الرجال في السودان. يعرف معدل البقاء علي قيد الحياة لمدة خمس سنوات علي انه نسبة المرضي اللذين يظلون علي قيد الحياة لخمس سنوات من تشخيصهم للمرض لتقييم كفاءة التشخيص والعلاج. هنالك عدة طرق لحساب معدل البقاء خمس سنوات لمريض السرطان منها عن طريق حساب النسبة مباشرة او باستخام طريقة المشاهدة او الطريقة المعدلة او طريقة التوقع. الهدف الاساسي من البحث دراسة العوامل المؤثرة علي البقاء علي قيد الحياة لخمس سنوات لمريض سرطان البروستاتا في السودان, أجريت هذه الدراسة في السودان من يوليو 2013 الي يونيو 2017 وتشتمل علي 1177 مريض سرطان بروستاتا وتمت دراستهم لمعرفة اكثر الاعمار والمناطق والحاله الاجتماعية وعلاقه القرابة بين الابوين للمريضي اللذين تم تسجيلهم لدي مكتب الاحصاء في المركز القومي لعلاج الاورام بالخرطوم من يناير 2010 الي ديسمبر 2012. تمت متابعه 306 مريض سرطان بروستاتا لحساب معدل البقاء لمدة خمس سنوات لمعرفه من ظل علي قيد الحياة منهم. وجد من خلال الطريقه المباشرة حوالي 111 (36.3%) من 306 مريض كانو علي قيد الحياة لخمس سنوات من تاريخ اول يوم لبدأ العلاج. لحساب معدل البقاءلخمس سنوات لمرضي سرطان البروستاتا ذوي الاعمار من 45 الي 97 بالمشاهدة وو الطريقة المعدلة والتوقع و ذلك باستخدام طريقة كوبلن وملير، كانت النتائج (39%)، (42%) و (44%) علي التوالي . وجد من خلال هذه الدراسة ان هنالك عدة عوامل تؤثر علي معدل بقاء المريض علي قيد الحياة لخمس سنوات مثل العمر ونوع العلاج ومراحله ومنطقة انتشار المرض. في الختام بالامكان حساب معدل البقاء علي قيد الحياة لمرضي سرطان البروستاتا السودانيين بالمعادلة التالية: معدل البقاء =

(مرحلة المرض × 1.396-) + (نوع العلاج المستخدم × 0.19) + (منطقه الانتشار في الجسم × 0.105-) + 6.53

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Abbreviations

5YSR	Five Years Survival Rate
Tc^{99m}	Technetium-99 is a Metastable
DHT	Dihydrotestosterone
BPH	Benign prostatic hyperplasia
ACS	American Cancer Society
PSA	Prostate Specific Antigen
pH	Potential Of Hydrogen
FGF	Fibroblast Growth Factor
DRE	Digital Rectal Examination
CT	Computed Tomography
MRI	Magnetic Resonance Imaging
ng/mL	Nanograms Per Millilitre
FNA	Fine Needle Aspiration
TRUS	Transrectal Ultrasound
ADT	Androgen Deprivation Therapy
PAP	Prostatic Acid Phosphatase

IV	Intravenous
EBRT	External Beam Radiation Therapy
DICOM	Digital Imaging and Communications in Medicine
^{99m} Tc MDP	*Technetium 99m*-Methyl Diphosphonate
mCi	Millicurie
MBq	Megabecquerel
kg	Kilogram
NCI	National Cancer Institute
AJCC	American Joint Committee on Cancer
MITS	Metastasis
CaPSURE	Cancer of the Prostate Strategic Urologic Research Endeavor.

Chapter one
Introduction

1.1 Introduction:

The five-year survival rate has been used to assess the prognosis of disease, normally calculated from the point of diagnosis. its define as the percentage of patients alive five years after the disease is diagnosed and used to evaluate the effectiveness of treatments (Gordis, 2008) . There are many methods to calculate the five-year survival rate in my thesis used direct method to calculate the five years survival, observed survival rate, corrected survival rate and Relative survival rate.

Calculation by the direct method, its simplest method and briefly to determine patient survival is to calculate the percentage of patients alive at the end of five years, which is the ratio of all patients, were alive five years after their respective dates of first treatment to the total number of subjects (Gordis, 2008).

Calculation by Observed survival, the direct method for calculating a survival rate does not use all the information available for example some patient died in the second year after treatment was started and other patient lived for more than four years. such information should be useful, The actuarial, or life-table, method provides a means for using all the follow-up information accumulated up to the closing date of the study. The actuarial method has the further advantage of providing information on the survival pattern, that is, the manner in which the patient group was depleted during the total period of observation define is rating of the probability of surviving all causes of death. Calculated by the life-table method (Cutler &Ederer, 1958).

Calculation by Corrected Survival Rate, the observed survival rate calculated for all deaths, not indicates the cause of death, may be some patients died by other

reason. Whenever reliable information on cause of death is available, a correction survival rate can be made for deaths due to causes other than the disease under study (Cutler &Ederer, 1958).

Calculation by Relative Survival Rate, the Information on cause of death is sometimes unavailable or unreliable. In this case, cannot depend on a corrected survival rate. Can calculate the survival rate by relative survival rate, which is the ratio of the observed survival rate to the expected rate for a group of people in the general population similar to the patient group with respect to race, sex, age and calendar period of observation (Cutler &Ederer, 1958).

Prostate cancer is most of common cancer in world; it ranked second among all cancers in both sexes after breast (Ferlay, et al,2012). And its the most common cancer in Sudanese men (Khalid, et al,2012). In people with prostate cancer, the bone is often the first distant site of cancer spread. More than 2 out of 3 prostate cancers that spread to other parts of the body spread to the bones (Fizazi, et al, 2011).

Bone is a common site for metastasis owing to high blood flow in the red marrow; the presence of adhesive molecules on tumor cells that bind them to stromal cells in the bone marrow; and the production of angiogenic factors and bone-resorbing factors that enhance tumor growth, thereby providing access to the resorbed bone matrix for subsequent tumor adhesion and proliferation Roodman GD. Mechanisms of bone metastasis (Suva, et al . 2009).

To detect the bones metastasis use Nuclear medicine Modality, the most common radiotracers used in bone scanning include Tc-99m MDP and F-18 NaF. Tc-99m MDP is used for gamma camera imaging. The standard adult dose is approximately 740 MBq. Tc-99m emits 140 keV gamma rays upon decay, and these gamma rays are detected by nuclear gamma cameras to allow localizing where the Tc-99m travels within the body. For imaging bone metabolism, the radionuclide is usually

attached to medronic acid (methylene diphosphonate). Caution is recommended when it is used in pregnant or nursing women. There have been rare reports of allergic reactions to Tc-99m MDP, and medical equipment should be available to treat severe reactions (GE Healthcare. 2007)

1.2 Problem of the study:

Prostate cancer is most of common cancer in world; it ranked second among all cancers in both genders after breast (Ferlay, et al, 2012) It also the most common cancer in Sudanese men (Khalid, et al, 2012). In people with prostate cancer, the bone is often the first distant site of cancer spread. More than 2 out of 3 prostate cancers that spread to other parts of the body spread to the bones (Fizazi,2011). Advances in the diagnosis and treatment of prostate cancer can help to improve the survival rate. This situation lead to variability in treatment options, site of MITS, Age, type of cancer cells and grading of cancer as well as the 5YSR, therefore if we can quantify the factor affecting the 5YSR it will be possible to estimate the 5YSR and hence the factors that enhance the 5YSR.

1.3. Significance of the study:

The early detection of prostate cancer and choose the best option of treatment can help in improvement of the survival rate for patient with prostate cancer.

1.4 Objective of the study:

Study of the factors influencing five year survival rate of Patient with Prostate Cancer in Sudan

Specific objectives:

- To determine the Five Years Survival Rate for Prostate cancer among Sudanese patient.

- To evaluate the metastasis from prostate cancer with grade of tumor.
- To assess the relationship between Age, grade, type of cancer cell with survival rate.
- To map cancer of prostate in Sudan
- To assess the effectiveness of treatment option.
- To find an empirical equation for 5YSR estimation

1.5 overview of the study:

This study falls into five chapters; chapter one is an introduction, which includes the problem of the study, objectives, significance of the study, and overview. Chapter two is a literature review which includes theoretical background and previous studies. While chapter three is a methodology that includes material and methods, and chapter four includes the results presentation and finally chapter five includes discussion, conclusion and recommendations.

Chapter two

Theoretical background & Literature review

2.1 Anatomy of prostate gland:

The prostate (from Ancient Greek προστάτης, prostates, literally "one who stands before", "protector", "guardian" (Harper, Douglas 2013) is a compound tubuloalveolar exocrine gland of the male reproductive system in most mammals.(Romer,Parsons,1977)It differs considerably among species anatomically, chemically, and physiologically.

The function of the prostate is to secrete a slightly alkaline fluid, milky or white in appearance, that in humans usually constitutes roughly 30% of the volume of the semen along with spermatozoa and seminal vesicle fluid(Am J Physiol. 136 (3)). Semen is made alkaline overall with the secretions from the other contributing glands, including, at least, the seminal vesicle fluid (Semen analysis 2009). The alkalinity of semen helps neutralize the acidity of the vaginal tract, prolonging the lifespan of sperm. The prostatic fluid is expelled in the first ejaculate fractions, together with most of the spermatozoa. In comparison with the few spermatozoa expelled together with mainly seminal vesicular fluid, those expelled in prostatic fluid have better motility, longer survival and better protection of the genetic material.

2.1.1 Structure:

A healthy human male prostate is classically said to be slightly larger than a walnut. The mean weight of the normal prostate in adult males is about 11 grams, usually ranging between 7 and 16 grams.(Leissner,1979). The prostate can be divided in two ways: by zone, or by lobe It is sheathed in the muscles of the pelvic floor, which contract during the ejaculatory process (Instant 2007) .

2.1.1.1 Zones:

The "zone" classification is more often used in pathology. The idea of "zones" was first proposed by John E. McNeal in 1968. McNeal found that the relatively homogeneous cut surface of an adult prostate in no way resembled "lobes" and thus led to the description of "zones"(Myers, Robert P (2000))

The prostate gland has four distinct glandular regions, two of which arise from different segments of the prostatic urethra:

Table (2.1): The "zone" classification in prostate gland

Name	Fraction of gland	Description
Peripheral zone (PZ)	Up to 70% in young men	The sub-capsular portion of the posterior aspect of the prostate gland that surrounds the distal urethra. It is from this portion of the gland that ~70–80% of prostatic cancers originate.(**Prostate Cancer Information 2010**)
Central zone (CZ)	Approximately 25% normally	This zone surrounds the ejaculatory ducts. The central zone accounts for roughly 2.5% of prostate cancers although these cancers tend to be more aggressive and more likely to invade the seminal vesicles(**Cohen RJ et all (2008**).
Transition zone (TZ)	5% at puberty	~10–20% of prostate cancers originate in this zone. The transition zone surrounds the proximal urethra and is the region of the prostate gland that grows throughout life and is responsible for the disease of benign prostatic enlargement. (**Prostate Cancer Information 2010**)
Anterior fibro-muscular zone (or stroma)	Approximately 5%	This zone is usually devoid of glandular components, and composed only, as its name suggests, of muscle and fibrous tissue.

2.1.1.2 Lobes:

The "lobe" classification is more often used in anatomy.

Table (2.2): The "lobe" classification in prostate gland

Anterior lobe (or isthmus)	roughly corresponds to part of transitional zone
Posterior lobe	roughly corresponds to peripheral zone
Lateral lobes	spans all zones
Median lobe (or middle lobe)	roughly corresponds to part of central zone

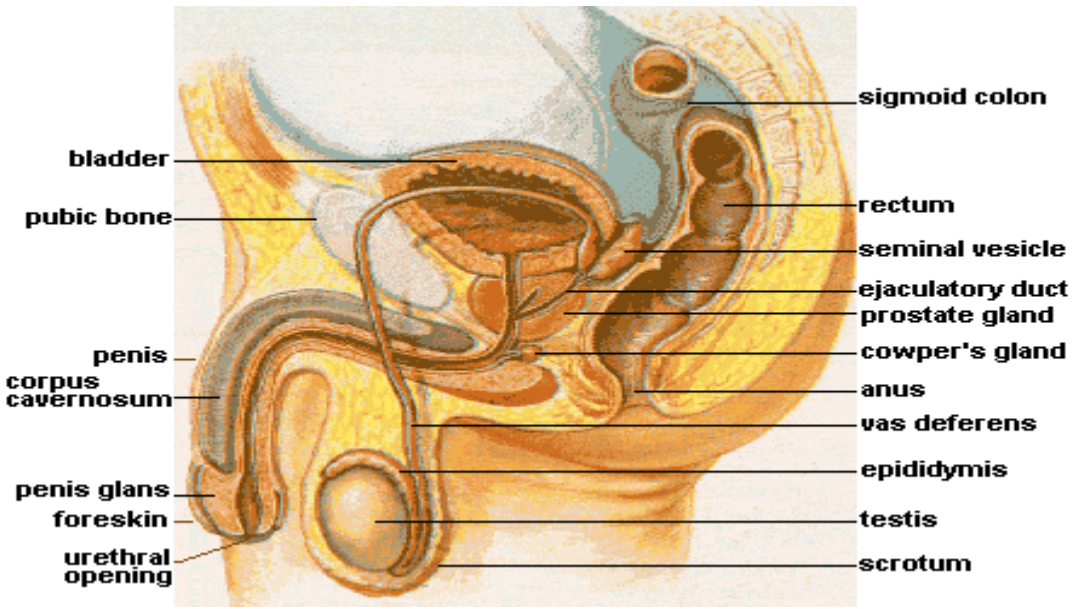
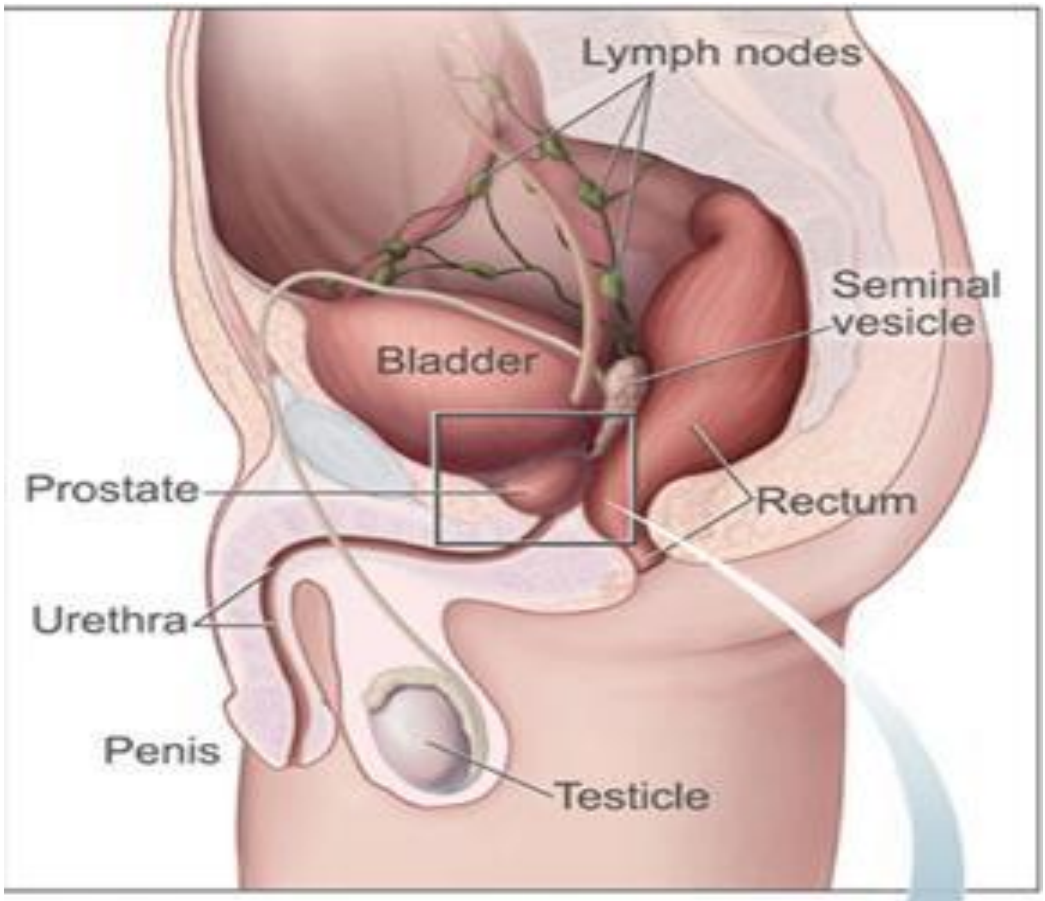
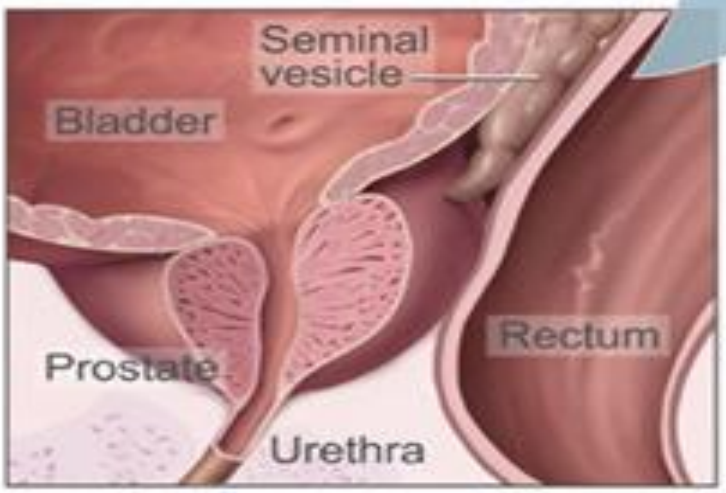


Figure (2.1): The relations of the Prostate Gland with other organs in pelvis area.

(Gray, 1918)



This shows the prostate and nearby organs.



This shows the inside of the prostate, urethra, rectum, and bladder.

Figure (2.2): Show the inside of the prostate and nearby organs. **(**Gray, 1918)

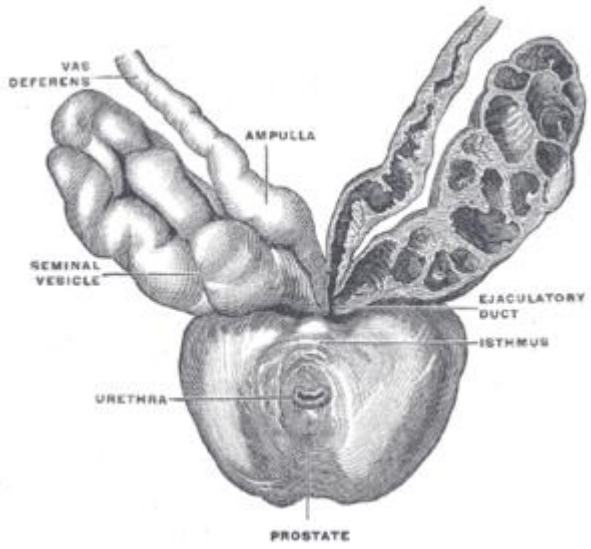


Figure: (2.3): Prostate with seminal vesicles and seminal ducts, viewed from in front and above (Gray, 1918)

2.1.2 The histology of Prostate:

The prostate gland has three types of cells:

- Glandular cells
- Myoepithelial cells
- Subepithelial interstitial cells (Lerut T, et al, (2014).

2.1.3 The Function of Prostate:

Male sexual response during male ejaculation, sperm is transmitted from the vas deferens into the male urethra via the ejaculatory ducts, which lie within the prostate gland. It is possible for some men to achieve orgasm solely through stimulation of the prostate gland, such as prostate massage or receptive anal intercourse(Martha (2012)

Secretions, Prostatic secretions vary among species. They are generally composed of simple sugars and are often slightly alkaline. In human prostatic secretions, the

protein content is less than 1% and includes proteolytic enzymes, prostatic acid phosphatase, beta-microseminoprotein, and prostate-specific antigen. The secretions also contain zinc with a concentration 500–1,000 times the concentration in blood. (Alan J., 2015)

Regulation, to function properly, the prostate needs male hormones (androgens), which are responsible for male sex characteristics. The main male hormone is testosterone, which is produced mainly by the testicles. It is dihydrotestosterone (DHT), a metabolite of testosterone that predominantly regulates the prostate

2.1.4 Clinical significance:

Prostatitis is inflammation of the prostate gland. There are primarily four different forms of prostatitis, each with different causes and outcomes. Two relatively uncommon forms, acute prostatitis and chronic bacterial prostatitis, are treated with antibiotics (category I and II, respectively). Chronic non-bacterial prostatitis or male chronic pelvic pain syndrome (category III), which comprises about 95% of prostatitis diagnoses, is treated by a large variety of modalities including alpha blockers (Quercetin, 2014.).

Benign prostatic hyperplasia (BPH) occurs in older men. the prostate often enlarges to the point where urination becomes difficult. Symptoms include needing to urinate often (frequency) or taking a while to get started (hesitancy). If the prostate grows too large, it may constrict the urethra and impede the flow of urine, making urination difficult and painful and, in extreme cases, completely impossible (Verhamme KM, 2002).

Prostate cancer is one of the most common cancers affecting older men in developed countries and a significant cause of death for elderly men.(Estimated by some specialists at 3% [citation needed]). Despite this, the American Cancer

Society's position regarding early detection is "Research has not yet proven that the potential benefits of testing outweigh the harms of testing and treatment". They believe "that men should not be tested without learning about... the risks and possible benefits of testing and treatment" which should be discussed with a doctor at age 50 or at age 45 if the patient is black or has a father or brother who acquired prostate cancer before age 65.(American Cancer Society, 2011)

2.1.5 skene's gland:

Skene's gland, also known as the paraurethral gland, found in females, is homologous to the prostate gland in males. However, anatomically, the uterus is in the same position as the prostate gland. In 2002, Skene's gland was officially renamed to female prostate by the Federative International Committee on Anatomical Terminology.(Flam, Faye (2006).

The female prostate, like the male prostate, secretes PSA and levels of this antigen rise in the presence of carcinoma of the gland. The gland also expels fluid, like the male prostate, during orgasm.(Kratochvíl S., 1994).

2.2 Anatomy of Bones:

A bone is a rigid organ that constitutes part of the vertebrate skeleton. Bones support and protect the various organs of the body, produce red and white blood cells, store minerals, provide structure and support for the body, and enable mobility. Bones come in a variety of shapes and sizes and have a complex internal and external structure. They are lightweight yet strong and hard, and serve multiple functions. Bone tissue is a hard tissue, a type of dense connective tissue. It has a honeycomb-like matrix internally, which helps to give the bone rigidity. Bone tissue is made up of different types of bone cells. Osteoblastsandosteocytes are involved in the formation and mineralization of bone; osteoclasts are involved in the resorption of bone tissue. Modified (flattened)

osteoblasts become the lining cells that form a protective layer on the bone surface. The mineralised matrix of bone tissue has an organic component of mainlycollagen called ossein and an inorganic component of bone mineral made up of various salts. Bone tissue is a mineralized tissue of two types, cortical and cancellous bone. Other types of tissue found in bones include bone marrow, endosteum, periosteum, nerves, blood vessels and cartilage.

In the human body at birth, there are over 270 bones (Steele, (1988) but many of these fuse together during development, leaving a total of 206 separate bones in the adult not counting numerous small sesamoid bones. The largest bone in the body is the femur or thigh-bone, and the smallest is the stapes in the middle ear (Mammal anatomy, 2010) .

2.2.1 Types of Bones:

There are five types of bones in the human body: long, short, flat, irregular, and sesamoid.(Types of bone". mananatomy.com. 2016).

Long bones are characterized by a shaft, the diaphysis that is much longer than its width; and by an epiphysis, a rounded head at each end of the shaft. They are made up mostly of compact bone, with lesser amounts of marrow, located within the medullary cavity, and areas of spongy, cancellous bone at the ends of the bones. Most bones of the limbs, including those of the fingers and toes, are long bones. The exceptions are the eight carpal bones of the wrist, the seven articulating tarsal bones of the ankle and the sesamoid bone of the kneecap. Long bones such as the clavicle, that have a differently shaped shaft or ends, are also called modified long bones.

Short bones are roughly cube-shaped, and have only a thin layer of compact bone surrounding a spongy interior. The bones of the wrist and ankle are short bones.

Flat bones are thin and generally curved, with two parallel layers of compact bones sandwiching a layer of spongy bone. Most of the bones of the skull are flat bones, as is the sternum (Bart Clarke (2008)

Sesamoid bones are bones embedded in tendons. Since they act to hold the tendon further away from the joint, the angle of the tendon is increased and thus the leverage of the muscle is increased. Examples of sesamoid bones are the patella and the pisiform(Adriana Jerez, et al. 2010).

Irregular bones do not fit into the above categories. They consist of thin layers of compact bone surrounding a spongy interior. As implied by the name, their shapes are irregular and complicated. Often this irregular shape is due to their many centers of ossification or because they contain bony sinuses. The bones of the spine, pelvis, and some bones of the skull are irregular bones. Examples include the ethmoid and sphenoid bones (Pratt, Rebecca,2012)

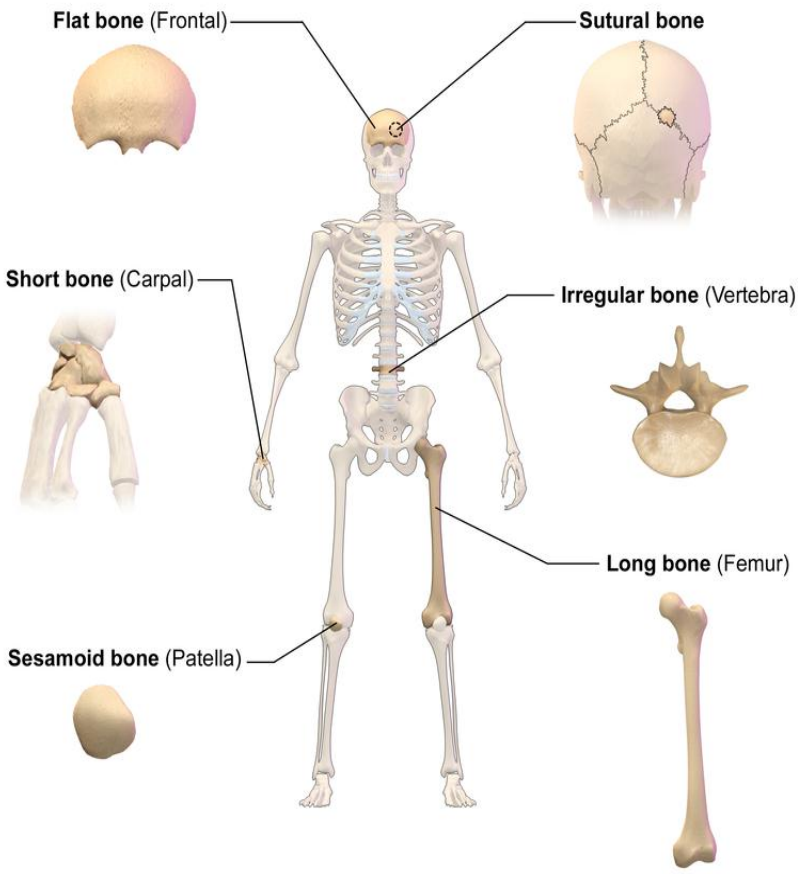


Figure: (2.4):show the Classification of Bones by shape (Gray, 1918)

2.2.2 Function of Bones:

- Mechanical

Bones serve a variety of mechanical functions. Together the bones in the body form the skeleton.

Bones protect internal organs, such as the skull protecting the brain or the ribs protecting the heart and lungs.

Mechanically, bones also have a special role in hearing. The ossicles are three small bones in the middle ear which are involved in sound transduction.

- Synthetic

Cancellous bones contain bone marrow. Bone marrow produces blood cells in a process called hematopoiesis. Blood cells that are created in bone marrow include red blood cells, platelets and white blood cells(Fernández, 2013).

- Metabolic

- Mineral storage — bones act as reserves of minerals important for the body, most notably calcium and phosphorus (Doyle, 2008).
- Growth factor storage — mineralized bone matrix stores important growth factors such as insulin-like growth factors, transforming growth factor, bone morphogenetic proteins and others.
- Fat storage — the yellow bone marrow acts as a storage reserve of fatty acids.
- Acid-base balance — bone buffers the blood against excessive pH changes by absorbing or releasing alkaline salts.
- Detoxification — bone tissues can also store heavy metals and other foreign elements, removing them from the blood and reducing their effects on other tissues. These can later be gradually released for excretion.
- Endocrine organ — bone controls phosphate metabolism by releasing fibroblast growth factor – 23 (FGF-23), which acts on kidneys to reduce phosphate reabsorption. Bone cells also release a hormone called osteocalcin, which contributes to the regulation of blood sugar (glucose) and fat deposition. Osteocalcin increases both the insulin secretion and sensitivity, in addition to boosting the number of insulin-producing cells and reducing stores of fat (Lee, et al.2007)
- Calcium balance—the process of bone resorption by the osteoclasts releases

stored calcium into the systemic circulation and is an important process in regulating calcium balance. As bone formation actively fixes circulating calcium in its mineral form, removing it from the bloodstream, resorption actively unfixes it thereby increasing circulating calcium levels. These processes occur in tandem at site-specific locations.

2.2.3 Clinical significance

A number of diseases can affect bone, including arthritis, fractures, infections, osteoporosis and tumours. Conditions relating to bone can be managed by a variety of doctors, including rheumatologists for joints, and orthopedic surgeons, who may conduct surgery to fix broken bones. Other doctors, such as rehabilitation specialists may be involved in recovery, radiologists in interpreting the findings on imaging, and pathologists in investigating the cause of the disease, and family doctors may play a role in preventing complications of bone disease such as osteoporosis.

When a doctor sees a patient, a history and exam will be taken. Bones are then often imaged, called radiography. This might include ultrasound X-ray, CT scan, MRI scan and other imaging such as a Bone scan, which may be used to investigate cancer (Britton 2010).

2.2.3.1 Fractures

In normal bone, fractures occur when there is significant force applied, or repetitive trauma over a long time. Fractures can also occur when a bone is weakened, such as with osteoporosis, or when there is a structural problem, such as when the bone remodels excessively (such as Paget's disease) or is the site of the growth of cancer (Britton 2010).

2.2.3.1 Tumour

There are several types of tumour that can affect bone; examples of benign bonetumours include osteoma, osteoidosteoma, osteochondroma, osteoblastoma, enchondroma, giant cell tumor of bone, and aneurysmal bone cyst

2.2.3.2 Cancer:

Cancer can arise in bone tissue, and bones are also a common site for other cancers to spread (metastasize) to. Cancers that arise in bone are called "primary" cancers, although such cancers are rare. Metastases within bone are "secondary" cancers, with the most common being breast cancer, lung cancer, prostate cancer, thyroid cancer, and kidney cancer. Secondary cancers that affect bone can either destroy bone (called a "lytic" cancer) or create bone (a "sclerotic" cancer). Cancers of the bone marrow inside the bone can also affect bone tissue, examples including leukemia and multiple myeloma. Bone may also be affected by cancers in other parts of the body. Cancers in other parts of the body may release parathyroid hormone or parathyroid hormone-related peptide. This increases bone reabsorption, and can lead to bone fractures (Britton 2010).

2.2.3.3 Osteoporosis:

Osteoporosis is a disease of bone where there is reduced bone mineral density, increasing the likelihood of fractures (Britton 2010).

2.4 investigations:

2.4.1Prostate Cancer:

Prostate cancer is the most common noncutaneous cancer among males, making the diagnosis and staging of this cancer of great medical and public interest.

- **Screening controversies**

Digital rectal examination (DRE) and PSA evaluation are the two components necessary for a modern screening prostate cancer program. However, there is controversy regarding screening.

- **Laboratory studies**

  ✓ PSA screening: Controversy exists regarding PSA level cutoffs and reference ranges

  ✓ DRE: Serial examinations are best; clues to the patient's condition in conjunction with PSA levels include presence of a nodule, as well as asymmetry, texture difference(s), and bogginess of the prostate, seminal vesicles, and adjacent organs

  ✓ Biopsy and histologic examination: These aid in the diagnosis and help to determine the Gleason score; a biopsy can also help differentiate a cyst or calculus from cancer foci

- Imaging studies

  ✓ Computed tomography (CT) scanning: To assess extension into the bladder and lymph nodes for staging the cancer or for considering pretreatment lymph node sampling

  ✓ Endorectal magnetic resonance imaging (MRI): To localize cancer within the prostate and seminal vesicles; to help in local staging

  ✓ Bone scanning: To evaluate bone metastasis

  ✓ MRI: To determine the etiology of questionable lesions found on bone scans

  ✓ Transrectal ultrasonography: To examine the prostate for hypoechoic areas, which are commonly associated with cancers but are not specific enough for diagnostic purposes.

Men with PSA levels above 10 ng/mL, high-grade histology (Gleason score

of ≥7), or physical findings suggesting stage T3 disease should probably undergo a staging CT scan and bone scan. Neither CT scanning nor MRI can be used to determine if lymph nodes are reactive or contain malignant deposits, unless the nodes are significantly enlarged and a percutaneous biopsy can be performed (Lanna Cheuck,2016)

2.4.2 Bone Cancer:

- Imaging tests to detect bone cancer by X-rays

Most bone cancers show up on x-rays of the bone. The bone at the site of the cancer may appear "ragged" instead of solid. The cancer can also appear as a hole in the bone. Sometimes doctors can see a tumor around the defect in the bone that might extend into nearby tissues (such as muscle or fat). The radiologist (doctor who specializes in reading x-rays) can often tell if a tumor is malignant by the way it appears on the x-ray, but only a biopsy can absolutely determine that. A chest x-ray is often done to see if bone cancer has spread to the lungs(ACS.2016).

- Computed tomography (CT) scans

CT scans are helpful in staging cancer. They help tell if your bone cancer has spread into your lungs, liver, or other organs. These scans also show the lymph nodes and distant organs where metastatic cancer might be present. CT scans can also be used to precisely guide a biopsy needle into a suspected metastasis. For this procedure, called a CT-guided needle biopsy, the patient remains on the CT scanning table while a radiologist advances a biopsy needle toward the location of the mass. CT scans are repeated until the doctors are confident that the needle is within the mass.(ACS.2016).

- Magnetic resonance imaging (MRI) scans

MRI scans are often the best test for outlining a bone tumor. They are also particularly helpful for looking at the brain and spinal cord. MRI scans are a little more uncomfortable than CT scans. First, they take longer -- often up to an hour. Also, you have to be placed inside a tube, which is confining and can upset people with claustrophobia (fear of enclosed spaces). The machine also makes a thumping noise that you may find disturbing. Some places provide headphones with music to block this out.(ACS.2016).

- **Radionuclide bone scans**

This procedure helps show if a cancer has spread to other bones. It can find metastases earlier than regular x-rays. Bone scans also can show how much damage the primary cancer has caused in the bone.For this test, the patient receives an injection of radioactive material called technetium diphosphonate . The amount of radioactivity used is very low and causes no long-term effects. This substance is attracted to diseased bone cells throughout the entire skeleton. Areas of diseased bone will be seen on the bone scan image as dense, gray to black areas, called "hot spots." These areas suggest metastatic cancer is present, but arthritis, infection, or other bone diseases can also cause a similar pattern. To distinguish among these conditions, the cancer care team may use other imaging tests or take bone biopsies.(ACS.2016).

- **Positron emission tomography (PET or PET) scans**

PET scans use glucose (a form of sugar) that contains a radioactive atom. A special camera can detect the radioactivity. Cancer cells absorb a lot of the radioactive sugar because of their high rate of metabolism. PET scans are useful in looking for cancer throughout your entire body. It can sometimes help tell if a tumor is cancerous or benign. It is being combined with CT scans to better pinpoint some kinds of cancer.(ACS.2016).

- **Biopsy**

A biopsy is a sample of tissue taken from a tumor so that it can be looked at under a microscope. This is the only way to know that the tumor is cancer and not some other bone disease. If cancer is present, the biopsy can tell the doctor if it is a primary bone cancer or cancer that started somewhere else and spread to the bone (metastasis). Several types of tissue and cell samples are used to diagnose bone cancer. It is very important a surgeon with experience in diagnosing and treating bone tumors do the biopsy procedure. The surgeon will choose a biopsy method based on whether the tumor looks benign or malignant and exactly what type of tumor is most likely (based on the bone x-rays, the patient's age, and the location of the tumor). Some kinds of bone tumors can be recognized from needle biopsy samples, but larger samples (from a surgical biopsy) are often needed to diagnose other types. Whether the surgeon plans to remove the entire tumor at the time of the biopsy will also influence the choice of biopsy type. The wrong kind of biopsy can sometimes make it hard later for the surgeon to remove all of the cancer without having to also remove all or part of the arm or leg containing the tumor. It also may cause the cancer to spread.(ACS.2016).

- **Needle biopsy**

There are 2 types of needle biopsies: fine needle biopsies and core needle biopsies. For both types, a local anesthetic is first used to numb the area for the biopsy. For fine needle aspiration (FNA), the doctor uses a very thin needle attached to a syringe to withdraw a small amount of fluid and some cells from the tumor mass. Sometimes, the doctor can aim the needle by feeling the suspicious tumor or area that is near the surface of the body. If the tumor cannot be felt because it is too deep, the doctor can guide the needle while viewing a CT scan. This is called a CT guided needle biopsy and it is often done by an x-ray specialist known as an interventional radiologist. In a core needle biopsy, the doctor uses a

larger needle to remove a small cylinder of tissue (about 1/16 inch in diameter and 1/2 inch long). Many experts feel that a core needle biopsy is better than FNA to diagnose a primary bone cancer.

- **Surgical bone biopsy**

In this procedure, a surgeon needs to cut through the skin to reach the tumor in order to remove a small piece of tissue. This is also called an incisional biopsy. If the entire tumor is removed (not just a small piece), it is called an excisional biopsy. These biopsies are often done with the patient under general anesthesia (asleep). They can also be done using a nerve block, which numbs a large area. If this type of biopsy is needed, it is important that the surgeon who will later remove the cancer also be the one to do the biopsy.

2.5 Staging and Grading of prostate cancer:

2.5.1 *Staging:*

2.5.1.1*Tumor* [6]:

- T – Primary tumor
- TX – Primary tumor cannot be assessed
- T0 – No evidence of primary tumor
- T1 – Clinically inapparent tumor not palpable or visible by imaging
- T1a – Tumor incidental histologic finding in 5% or less of tissue resected
- T1b – Tumor incidental histologic finding in greater than 5% of tissue resected
- T1c – Tumor identified by needle biopsy (due to elevated prostate-specific antigen [PSA] level); tumors found in 1 or both lobes by needle biopsy but not palpable or reliably visible by imaging
- T2 – Tumor confined within prostate

- T2a – Tumor involving less than half a lobe
- T2b – Tumor involving 1 lobe or less
- T2c – Tumor involving both lobes
- T3 – Tumor extending through the prostatic capsule; no invasion into the prostatic apex or into, but not beyond, the prostatic capsule
- T3a – Extracapsular extension (unilateral or bilateral)
- T3b – Tumor invading seminal vesicle(s)
- T4 – Tumor fixed or invading adjacent structures other than seminal vesicles (eg, bladder neck, external sphincter, rectum, levator muscles, pelvic wall)
- NX – Regional lymph nodes (cannot be assessed)
- N0 – No regional lymph node metastasis
- N1 – Metastasis in regional lymph node or nodes

2.5.1.2 *Regional lymph nodes* (Green, 2002).

Regional lymph nodes are assessed via surgical removal or through biopsy of the pelvic lymph nodes, including the obturator chain. The surgical boundaries include the bifurcation of the common iliac, the obturator nerve, and the node of Cloquet.

2.5.1.3 Distant metastasis (Green, 2002).

- PM1c – More than 1 site of metastasis present
- MX – Distant metastasis cannot be assessed
- M0 – No distant metastasis
- M1 – Distant metastasis
- M1a – Nonregional lymph node(s)
- M1b – Bone(s)
- M1c – Other site(s)

2.5.2 *Stage groupings*:

The TNM system for grouping prostate cancer is based on the following 5 key pieces of information (ACS, 2015).

- The extent of the primary tumor (T category)
- Whether the cancer has spread to nearby lymph nodes (N category)
- The absence or presence of distant metastasis (M category)
- The PSA level at the time of diagnosis

Stage I - Cancer found in the prostate only

- T1, N0, M0, Gleason score 6 or less, PSA less than 10 or
- T2a, N0, M0, Gleason score 6 or less, PSA less than 10

Stage II (IIa and IIb) - Cancer is more advanced than stage I, but has not spread outside the prostate

Stage IIa - One of the following applies:

- T1, N0, M0, Gleason score of 7, PSA less than 20 or
- T1, N0, M0, Gleason score of 6 or less, PSA at least 10 but less than 20 or
- T2a or T2b, N0, M0, Gleason score of 7 or less, PSA less than 20

Stage IIb - One of the following applies:

- T2c, N0, M0, any Gleason score, any PSA or
- T1 or T2, N0, M0, any Gleason score, PSA of 20 or more or
- T1 or T2, N0, M0, Gleason score of 8 or higher, any PSA

Stage III - Cancer has spread outside the prostate and may have invaded the seminal vesicles

- T3, N0, M0, any Gleason score, any PSA

Stage IV - Cancer has spread outside the prostate, into surrounding pelvic organs, into lymph nodes, or as distant metastasis outside the pelvis

- T4, N0, M0, any Gleason score, any PSA or
- Any T, N1, M0, any Gleason score, any PSA or
- Any T, any N, M1, any Gleason score, any PSA

2.5.3 Gleason scores for grading prostate cancer:

Prostate cancer is also given a grade called a Gleason score. This score is based on how much the cancer looks like healthy tissue when viewed under a microscope. Less aggressive tumors generally look more like healthy tissue. Tumors that are more aggressive are likely to grow and spread to other parts of the body. They look less like healthy tissue

- Gleason X: The Gleason score cannot be determined.
- Gleason 6 or lower: The cells are well differentiated, meaning they look similar to healthy cells.
- Gleason 7: The cells are moderately differentiated, meaning they look somewhat similar to healthy cells.
- Gleason 8, 9, or 10: The cells are poorly differentiated or undifferentiated, meaning they look very different from healthy cells.

2.6 The treatment options of prostate cancer:

Depending on each case, treatment options for men with prostate cancer might include:

2.6.1 Surgery:

Surgery is a common choice to try to cure prostate cancer if it is not thought to have spread outside the prostate gland.
The main type of surgery for prostate cancer is a radical prostatectomy. In this operation, the surgeon removes the entire prostate gland plus some of the tissue around it, including the seminal vesicles. A radical prostatectomy can be done in different ways.

- Open approaches to radical prostatectomy

In the more traditional approach to doing a prostatectomy, the surgeon operates through a single long skin incision (cut) to remove the prostate and nearby tissues. This type of surgery, sometimes referred to as an open approach, is now done less often than in the past.

- Laparoscopic approaches to radical prostatectomy

Laparoscopic approaches use several smaller incisions and special long surgical tools to remove the prostate. The surgeon either holds the tools directly, or uses a control panel to precisely move robotic arms that hold the tools. This approach to prostatectomy has become more common in recent years.

If you're thinking about treatment with laparoscopic surgery, it’s important to understand what is known and what is not yet known about this approach. The most important factors are likely to be the skill and experience of your surgeon. If you decide that laparoscopic surgery is the right treatment for you, be sure to find a surgeon with a lot of experience

2.6.2 Radiation Therapy for Prostate Cancer:

Radiation therapy uses high-energy rays or particles to kill cancer cells.

Radiation may be used:

As the first treatment for cancer that is still just in the prostate gland and is low grade. Cure rates for men with these types of cancers are about the same as those for men treated with radical prostatectomy.

As part of the first treatment (along with hormone therapy) for cancers that have grown outside the prostate gland and into nearby tissues.

If the cancer is not removed completely or comes back (recurs) in the area of the prostate after surgery.

If the cancer is advanced, to help keep the cancer under control for as long as possible and to help prevent or relieve symptoms.

- Types of radiation therapy

The 2 main types of radiation therapy used for prostate cancer are:

- ✓ External beam radiation
- ✓ Brachytherapy (internal radiation

2.6.3Cryotherapy for Prostate Cancer

Cryotherapy (also called cryosurgery or cryoablation) is the use of very cold temperatures to freeze and kill prostate cancer cells. Despite it sometimes being called cryosurgery, it is not actually a type of surgery.

This type of procedure requires spinal or epidural anesthesia (the lower half of your body is numbed) or general anesthesia (you are asleep).

The doctor uses transrectal ultrasound (TRUS) to guide several hollow probes (needles) through the skin between the anus and scrotum and into the prostate. Very cold gases are then passed through the needles to freeze and destroy the prostate. To be sure the prostate is destroyed without too much damage to nearby tissues, the doctor carefully watches the ultrasound during the procedure. Warm saltwater is circulated through a catheter in the urethra during the procedure to keep it from freezing. The catheter is left in place for several weeks afterward to allow the bladder to empty while you recover.

After the procedure, you might need to stay in the hospital overnight, but many patients leave the same day.

Cryotherapy is less invasive than surgery, so there is usually less blood loss, a shorter hospital stay, shorter recovery period, and less pain. But compared with surgery or radiation therapy, doctors know much less about the long-term effectiveness of cryotherapy. Cryotherapy doesn’t appear to be as good as radiation for more advanced prostate tumors.

2.6.3Hormone Therapy for Prostate Cancer:

Hormone therapy is also called androgen deprivation therapy (ADT) or androgen suppression therapy. The goal is to reduce levels of male hormones, called androgens, in the body, or to stop them from affecting prostate cancer cells. Androgens stimulate prostate cancer cells to grow. The main androgens in the body are testosterone and dihydrotestosterone (DHT). Most of the androgens are made by the testicles, but the adrenal glands (glands that sit above your kidneys) also make a small amount. Lowering androgen levels or stopping them from getting into prostate cancer cells often makes prostate cancers shrink or grow more slowly for a time. But hormone therapy alone does not cure prostate cancer.
Hormone therapy may be used:

- ✓ If the cancer has spread too far to be cured by surgery or radiation, or if you can't have these treatments for some other reason
- ✓ If the cancer remains or comes back after treatment with surgery or radiation therapy
- ✓ Along with radiation therapy as initial treatment if you are at higher risk of the cancer coming back after treatment (based on a high Gleason score, high PSA level, and/or growth of the cancer outside the prostate)
- ✓ Before radiation to try to shrink the cancer to make treatment more effective

2.6.4Chemotherapy for Prostate Cancer:

Chemotherapy (chemo) uses anti-cancer drugs injected into a vein or given by mouth. These drugs enter the bloodstream and go throughout the body, making this treatment potentially useful for cancers that have spread (metastasized) to distant organs.

Chemo is sometimes used if prostate cancer has spread outside the prostate gland and hormone therapy isn't working. Recent research has also shown that chemo might be helpful if given along with hormone therapy.
Chemo is not a standard treatment for early prostate cancer, but some studies are looking to see if it could be helpful if given for a short time after surgery.

2.6.5Vaccine Treatment for Prostate Cancer

Sipuleucel-T (Provenge) is a cancer vaccine. Unlike traditional vaccines, which boost the body's immune system to help prevent infections, this vaccine boosts the immune system to help it attack prostate cancer cells.
The vaccine is used to treat advanced prostate cancer that's no longer responding to hormone therapy but is causing few or no symptoms.
This vaccine is made specifically for each man. To make it, white blood cells (cells of the immune system) are removed from your blood over a few hours while you are hooked up to a special machine. The cells are then sent to a lab, where they are exposed to a protein from prostate cancer cells called prostatic acid phosphatase (PAP). The cells are then sent back to the doctor's office or hospital, where they are given back to you by infusion into a vein (IV). This process is repeated 2 more times, 2 weeks apart, so that you get 3 doses of cells. The cells help your other immune system cells attack the prostate cancer.
The vaccine hasn't been shown to stop prostate cancer from growing, but it seems to help men live an average of several months longer. As with hormone therapy and chemotherapy, this type of treatment has not been shown to cure prostate cancer.
Studies are now being done to see if this vaccine can help men with less advanced prostate cancer.

2.6.6Bone-directed treatment

Preventing and Treating Prostate Cancer Spread to Bones, if prostate cancer spreads to other parts of the body, it nearly always goes to the bones first. Bone metastasis can be painful and can cause other problems, such as fractures (breaks) or high blood calcium levels, which can be dangerous or even life threatening.
If the cancer has grown outside the prostate, preventing or slowing the spread of the cancer to the bones is a major goal of treatment. If the cancer has already reached the bones, controlling or relieving pain and other complications is also a very important part of treatment.
Treatments such as hormone therapy, chemotherapy, and vaccines may help with this, but other treatments more specifically target bone metastasis and the problems it may cause.

2.7 previous studies:

There are many studies all over the world were published and tackled the factors affects the five year survival rate of prostate cancer.
So I will tackle the theses that match with my main objectives. such as to calculate the survival rate andcorrelation with grade, Age,site of metastasis, type of cancer cells, the treatment and the mapping of prostate incidence in Sudan.

A Study Trends in US incidence and mortality rates for black and white Americans from 1975 to 2008 (Merrill, et al, 1999). Approximately 10% of the American population is black or African American. The overall American male prostate cancer incidence and mortality rates closely follow that of white men.

Prostate cancer incidence and mortality (1975–2007). Age-adjusted prostate cancer incidence and mortality rates per 100 000 for black and white Americans as measured in the National Cancer Institute Surveillance Epidemiology and End Results program.

A recent study carried out by Antonarakis ES, et al. in their work The natural history of metastatic progression in men with prostate-specific antigen recurrence after radical prostatectomy;Median follow-up after prostatectomy was 8.0 years, and after biochemical recurrence was 4.0 years. At last follow-up, 134 of 450 patients (29.8%) had developed metastases, while median MFS was 10.0 years. Using multivariable regressions, two variables emerged as independently predictive of MFS: PSA doubling time (<3.0 vs 3.0-8.9 vs 9.0-14.9 vs ≥15.0 months) and Gleason score (≤6 vs 7 vs 8-10). Using these stratifications of Gleason score and PSA doubling time, tables were constructed to predict median, 5- and 10-year MFS after PSA recurrence. In different patient subsets, median MFS ranged from 1 to 15 years. (Antonarakis ES, et al, 2012)

A study by American Cancer Society. Cancer Facts & Figures for African Americans 2013-2014. Atlanta. They showed that an estimated 35,430 cases of prostate cancer are expected to be newly diagnosed among African American men in 2013, accounting for 37% of all cancers diagnosed. It is estimated that 1 in 5 African American men will be diagnosed with prostate cancer in his lifetime. During 2005-2009, the average annual prostate cancer incidence rate among African American men was 228.8 cases per 100,000 men, which was 63% higher than the rate in white men . Similar to whites, incidence rates of prostate cancer in African American men increased sharply between 1989 and 1992, but have since been generally declining . The dramatic changes in prostate cancer incidence rates reflect the use of the prostate-specific antigen (PSA) blood test for the detection of prostate cancer. During 2000 to 2009, prostate cancer incidence rates dropped by 2.0% per year in African American men and 2.3% per year in whites **(A.C.S.,2013)**

Study by (Chin JL,et al) was performed on A total of 62 patients completed the trial. Median follow-up was 105.2 months (SD ±35.8). Accrual was limited due to newer data favoring longer neoadjuvant hormonal therapy and higher external beam radiotherapy dose for locally advanced prostate cancer. There was a greater reduction in prostate volume in the cryoablation group after intervention (-54% vs -34%, p ≤0.01). Disease specific survival and overall survival were comparable between the groups. However, the 8-year biochemical disease-free survival rate was significantly lower in the cryoablation group (17.4% vs 59.1%) (p = 0.01). (Chin JL,et al, 2012).

FizaziK,et al in their study Effectiveness of Bone Metastases Treatment by Sm-153 Oxabifore in Combination with Monoclonal Antibody Denosumab (Xgeva): they showed the Pain relief occurred within 4.4 ± 1.25 days (range 2-9 days) following Sm-153 oxabifore administration. The objective pain score decreased from 7.8 ± 0.5 to 0.2 ± 0.2 (range 0-1). This response to therapy was found to be statistically highly significant (P < 0.0001) (FizaziK,et al, 2009).

Moon K,et al in their theses Cancer incidence after localized therapy for prostate cancer.they showed Compared with men who received no prostate cancer-directed radiation, men who received external beam radiation therapy (EBRT) as their only form of radiation therapy had statistically significant increased odds of developing secondary cancers at several sites potentially related to radiation therapy, including the bladder (odds ratio [OR], 1.63; 95% confidence interval [95% CI], 1.44-1.84) and rectum (OR, 1.60; 95% CI, 1.29-1.99). Men who received EBRT also had statistically significant higher odds of developing secondary cancers at sites in the upper body and other areas not potentially related to radiation therapy, including the cecum (OR, 1.63; 95% CI, 1.10-1.70), transverse colon (OR, 1.85; 95% CI, 1.30-2.63), brain (OR, 1.83; 95% CI, 1.22-2.75), stomach (OR, 1.38; 95% CI, 1.09-1.75), melanoma (OR, 1.29; 95% CI, 1.09-1.53), and lung and bronchus (OR, 1.25; 95% CI, 1.13-1.37) compared with the odds among men who received no

radiation therapy. Men who received radiation therapy in the form of radioactive implants or isotopes, either in isolation or combined with beam radiation, did not have significantly different odds of secondary cancer occurring at any of the 20 most common sites.(Moon K,et al,2006)

Nelson CJ, et al in their study Cognitive effects of hormone therapy in men with prostate cancer. They found Testosterone and its derivatives may have an impact on cognition through several mechanisms in the brain, as supported by studies of animals and in aging men. Studies that researched the impact of androgen-deprivation therapy (ADT) on cognition in patients with prostate cancer patients were designed relatively well but suffered from small sample sizes. Between 47% and 69% of men on ADT declined in at least 1 cognitive area, most commonly in visuospatial abilities and executive functioning. Some studies reported contradictory results with increased functioning in verbal memory. (Nelson CJ, et al, 2008).

The study Intensive lifestyle changes may affect the progression of prostate cancer by OrnishD,et al, they showed none of the experimental group patients but 6 control patients underwent conventional treatment due to an increase in PSA and/or progression of disease on magnetic resonance imaging. PSA decreased 4% in the experimental group but increased 6% in the control group ($p = 0.016$). The growth of LNCaP(a cell line of human cells commonly used in the field of oncology) prostate cancer cells (American Type Culture Collection, Manassas, Virginia) was inhibited almost 8 times more by serum from the experimental than from the control group (70% vs 9%, $p < 0.001$). Changes in serum PSA and also in LNCaP cell growth were significantly associated with the degree of change in diet and lifestyle. (OrnishD, et al, 2005)

ScherHI,et al in their study Increased Survival with Enzalutamide in Prostate Cancer after Chemotherapy They founded enrolled 1199 patients who were randomly assigned to receive either enzalutamide (800 patients) or placebo (399 patients). The enrollment, follow-up, and data analysis of patients are shown in Fig. 1S in the Supplementary Appendix. Baseline characteristics were well matched between groups in terms of demographic characteristics, previous treatment history, and extent of disease .At the time of the interim analysis, the median time on treatment was 8.3 months in the enzalutamide group and 3.0 months in the placebo group. The median duration of follow-up to ascertain survival status was 14.4 months (Scher HI,et al, 2012)

The study impact of age at diagnosis on prostate cancer treatment and survival by Seth K., et al, they found about 13,805 men in CaPSURE, 12,286 had known primary treatment and at least 6 months of subsequent follow-up; of these, 496 had nonlocalized disease and were excluded, leaving 11,790. Baseline characteristics of the study , There was no consistent association between age and likelihood of missing data (11.4%, 20.0%, 10.1%, and 11.9% for men age ≤ 55, 56 to 65, 66 to 75, and > 75 years, respectively). Mean ± standard deviation age in the overall cohort was 66.2 ± 8.6 years, and median age was 66 years. Of these men 1,411 (12.0%) were age ≤ 55 years at the time of treatment, 4,005 (34.0%) were age 56 to 65, 4,667 (39.6%) were age 66 to 75, and 1,707 (14.5%) were older than age 75 years. The likelihood of high-risk disease by CAPRA classification increased significantly with increasing age cohort($P < .001$ by Mantel-Haenszel $\chi 2$) (Seth K., et al,2011)

Chapter three
Materials and methods

3.1 design of the study:

It is an analytical study where the data collected prospectively, which was performed in amongst the prostate cancer patients in Sudan

3.2 population of the study:

The target population for this research defined to include patient with prostate cancer duration (5) years.

3.3 study sample and type:

The study was a prospective study, about (1177) patients with prostate cancer.

3.4 Area and duration of the study:

The study was carried out in Radiation Isotopes center of Khartoum (RICK) in Sudan. The study started in July 2012 and finished in December 2016.

3.5 Tools & Equipment:

- To detect the metastasis of disease use the Single Photon Emission Computed Tomography (SPECT) (Siemens- dual head) with specifications.
    1. Dual Head variable angle
    2. SPECT & Whole body imaging capabilities.
    3. Image fusion software & hardware.
    4. Capable of acquiring multislicesSPECTscan.
    5. DICOM ready system
    6. Manufacturerto provide a comprehensive list of usersof dual head SPECT gamma camera
    7. Standard I.V. tray

8. Prism 2000XP or Axis camera fitted with LEHR collimator and Odyssey computer
9. ^{57}Co marker

3.6 Method & Technique

Bone scans remain as most sensitive imaging modality to detect osteoblastic response, as seen with fractures and osteoblastic metastatic disease, infections and metabolic disease. Before the scan there are procedures for equipment such as Perform Daily QC, Put LEHR collimators on detectors, check the (center and lock table on axis), Place sheet and pillow on patient table and Check camera energy window. After that prepare the patient by basic procedures such as no barium studies with in previous48 hours,Instruct patientto drink more water and empty bladder before scans. Theradiopharmaceutical is^{99m} Tc MDP 15 - 25 mCi (740 MBq - 925 MBq) with dose Adults 15- 25 mCi (740-925 MBq); Children - 200 μCi/kg (7.4 MBq/kg) (lower limits - 2 mCi) (74 MBq).

The procedures and technique

- ✓ The receptionistnotify technologists of patient's arrival
- ✓ The technologist or nurse prepared the dose
- ✓ Method of administration – intravenously
- ✓ Injection to imaging time – 2-4.5 hours.
- ✓ The patient removes any attenuation producing articles (jewelry, belt buckles, coins, large metal buttons, etc).
- ✓ Position patient on pallet. Left arm rest should be in position for patient. Put right arm rest in place. Remind patient to keep arms at his sides. Secure patient's feet together, if possible. This places the legs and hips in a true anterior position. Adjust patient's head in a true anterior and posterior position. Secure head, if necessary. Observe that patient is lying as flat as possible on the table. Pelvis should not be rotated. Both arms should be at the patient's sides

- ✓ Set up gantry for whole body imaging. Gantry moves to patient's feet.
- ✓ Set Head 1 height and linear travel position. Press Mark to locate end of scan.
- ✓ Move gantry to left.
- ✓ Adjust the patient or camera as necessary staying as close as possible with the detectors
- ✓ to start Set up computeroptions (time, mode matrix,etc)

3.7 Data analysis

The method of data analysis for general frequency % of age, Region, marital status, patient parents relative and incidence of all prostate cancer record in statistic office in RICK from January 2010 to December 2012 by data sheets will be symbolized, classified and analyzed by the computer (by using statistically package for social science (SPSS)

The complex tables will use in analysis & carried out the relationship between different variables and the important statistical indicators will be drawn from the study. The tables below to calculate the 5YSR by different method, Table (3.1) calculation by the direct method (see appendix).

Table (3.2): Calculation of observed survival rate, and its standard error, by the actuarial (life-table) method

(1) Year after Diagnosis (i)	(2) No. alive at Beginning of Year (l_i)	(3) No Dying During year (d_i)	(4) No. last seen Alive During Year (w_i)	(5) Effective No. Exposed to Risk of Dying (r_i)	(6) Proportion Dying During Year (q_i)	(7) Proportion Surviving year (p_i)	(8) Proportion Surviving From list Treatment to end year ($11p_i$)	(9) Entry (5) Minus Entry (3) ($r_i - d_i$)	(10) Entry(6) Divided By entry (9) $\frac{(q_i)}{r_i . d_i}$
0	**306**	**8**	**0**	**306.0**	**0.026**	**0.974**	**0.974**	**298**	**0.0000**
1	**298**	**73**	**1**	**297.5**	**0.245**	**0.755**	**0.735**	**224.5**	**0.2450**
2	**224**	**50**	**2**	**223.0**	**0.224**	**0.776**	**0.570**	**173**	**0.0013**
3	**172**	**31**	**2**	**171.0**	**0.181**	**0.819**	**0.467**	**140**	**0.0013**
4	**139**	**23**	**3**	**138.5**	**0.166**	**0.834**	**0.389**	**115.5**	**0.0014**
≥ 5	**113**	-	**113**	-	-	-		-	-
Total		**185**	**121**						**0.249**

$(r_i) = l_i - w_{i\ 2}$ $q_i = d_i r_i$ $p_i = 1 - q_i$

Table (3.3): Calculation of the corrected survival rate from the disease of interest

(1) Year after Diagnosis (i)	(2) No. alive at Beginning of Year (l_i)	(3) No Dying During year (d_i)		(4) No. last seen Alive During Year (w_i)	(5) Effective No. Exposed to Risk of Dying (r_i)	(6) Proportion Dying During Year (q_i)	(7) Proportion Surviving year (p_i)	(8) Proportion Surviving From list Treatment to end year ($11p_i$)
		(a) From Cancer ($d(c)_i$)	(b) From other causes ($d(o)_i$)					
0	306	6	2	0	305.0	0.020	0.980	0.980
1	298	69	4	1	295.5	0.234	0.766	0.751
2	224	46	4	2	221.0	0.208	0.792	0.595
3	172	28	3	2	168.5	0.166	0.834	0.496
4	139	21	2	3	136.5	0.154	0.846	0.420
≥ 5	113	-		113	-	-	-	
Total			185	121				

Where $(r_i)=l_i-w_i+(d(o)_i/2$ $q_i=(d(c)_i/r_i$ $p_i=1-q_i$

Table (3.4): Calculation of the relative cumulative survival rates among Prostate Cancer patients

(1) Year after Diagnosis (i)	(2) No. alive at Beginning of Year (l_i)	(3) No Dying During year (d_i)	(4) No. last seen Alive During Year (w_i)	(5) Effective No. Exposed to Risk of Dying (r_i)	(6) Proportion Dying During Year (q_i)	(7) Proportion Surviving year (p_i)	(8) Proportion Surviving From list Treatment to end year ($11p_i$)	(9) Relative survival rate ($11p_i/E_R$)
0	306	8	0	306.0	0.026	0.974	0.974	0.974
1	298	73	1	297.5	0.245	0.755	0.735	0.835
2	224	50	2	223.0	0.224	0.776	0.570	0.647
3	172	31	2	171.0	0.181	0.819	0.467	0.530
4	139	23	3	138.5	0.166	0.834	0.389	0.442
≥ 5	113	-	113	-	-	-		-
Total		185	121					

$(r_i)=l_i-w_i/2$ $q_i=d_ir_i$ $p_i=1-q_i$

E_R ***= Expected Survival Rate (0.88)***

3.8 Ethical approval

- ✓ Approved from the Republic of Sudan/Federal Ministry of Health/ Health Research Council/National Health Research Ethics Committee.
- ✓ Approved from the general manger of RICK
- ✓ Approved from Head of archiving department in RICK.
- ✓ Approved from Head of Nuclear medicine department in RICK.

Chapter four
Results

Section one: general frequency % of age, Region, marital status, patient parents relative and incidence of all prostate cancer record in statistic office in RICK from January 2010 to December 2012.

Table (4.1): shows the frequency % of the age group involved with Prostate Cancer from January 2010 to December 2012 in RICK (SUDAN)

Per year _	frequency	Age group Percentage %
20-34	3	00.25%
35-49	16	01.36%
50-64	245	20.82%
65-79	661	56.16%
80-94	247	21.00%
95-109	5	00.40%
Total	1177	

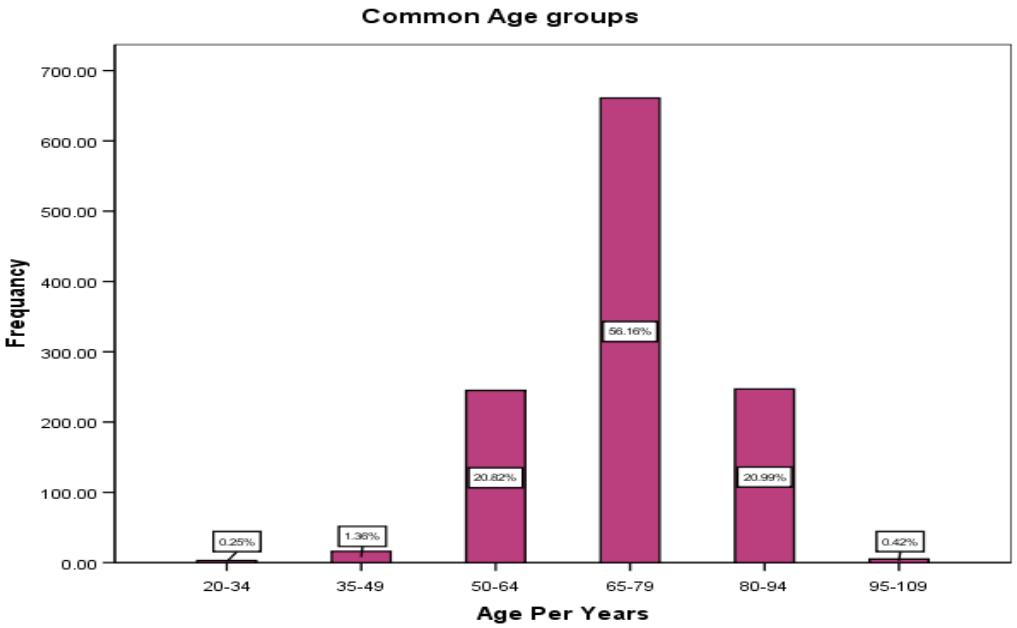
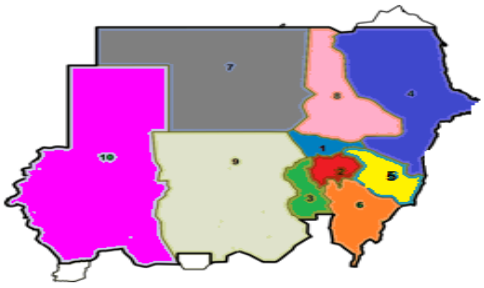


Figure (4.1) Bar graph shows the common age group involved with Ca. Prostate

Table (4.2): shows the frequency % of the state group involved with Prostate

Cancer from January 2010 to December 2012 in RICK (SUDAN)

State of Sudan	Frequency	Percentage %
Khartoum	226	19.20%
Aljazeera	109	9.26%
White Nile	96	8.16%
Red sea + Kaslaa	32	2.72%
Al qadarif	20	1.70%
Sinar +Damazin	62	5.27%
Northern	148	12.57%
River Nile	112	9.52%
Kordofan	194	16.48%
Darfur	157	13.34%
Other	21	1.78%
Total	1177	



code	Color	Incidence
1		19.20 %
2		9.26 %
3		8.16 %
4		2.72%
5		1.70 %
6		5.27 %
7		12.57 %
8		9.52 %
9		16.48 %
10		13.34 %
11		1.78%

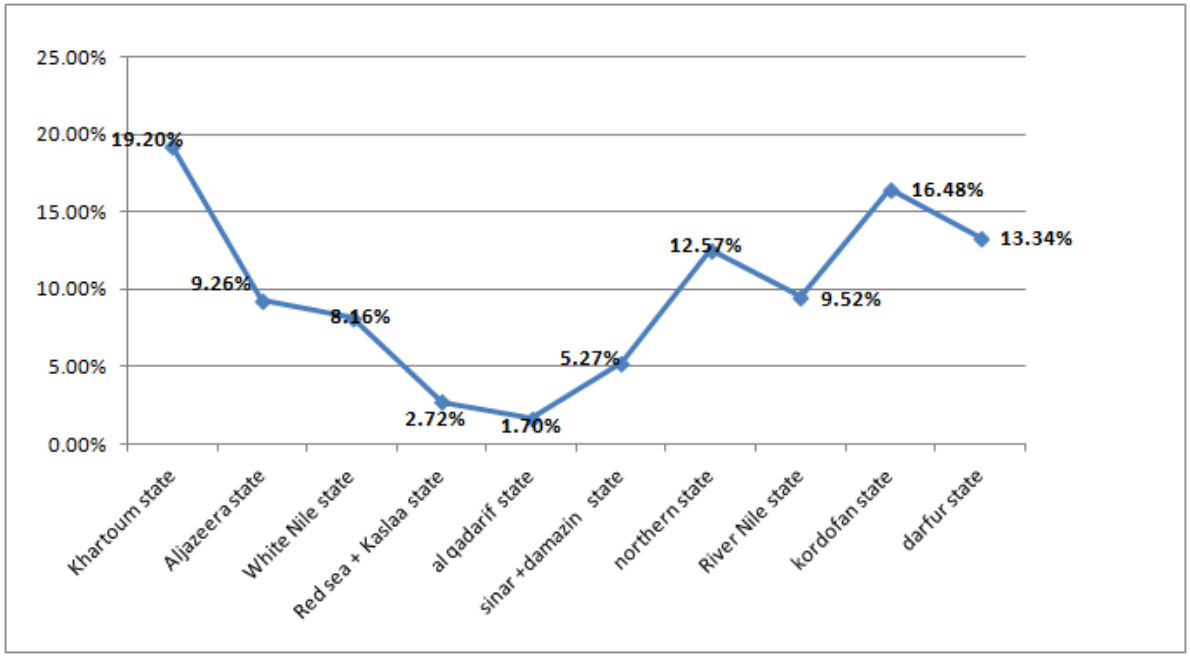


Figure (4.2) Line graph show the distribution of patient among state of Sudan.

Table (4.3): shows the frequency % of the Marital Status Group involved with Prostate Cancer from January 2010 to December 2012 in RICK (SUDAN)

Marital status	*Frequency*	*Percentage %*
Married	**1160**	**98.5%**
Single	**17**	**1.5%**
Total	**1177**	

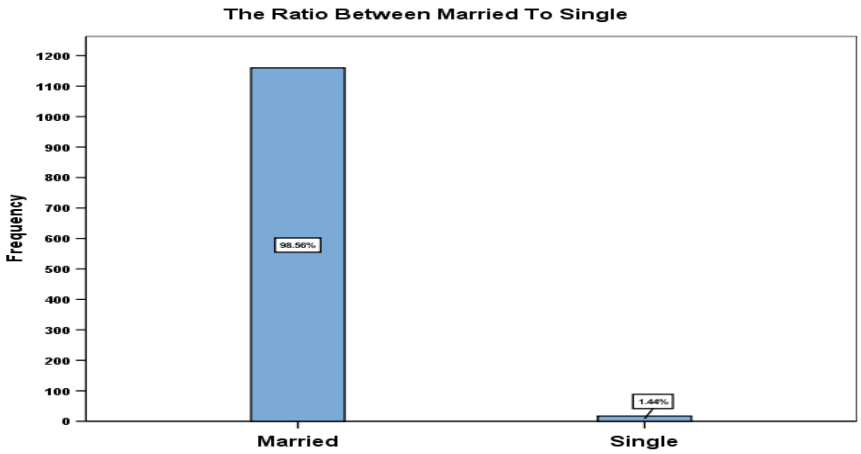


Figure (4.3) bar graph shows the ratio between married to signal among patients.

Table (4.4): shows the frequency % of the Patient Parents Relative Group involved with Prostate Cancer from January 2010 to December 2012 in RICK (SUDAN)

Patient parent's relative	*Frequency*	*Percentage %*
Relatives of the first degree	993	84.37%
Relatives of the second degree	103	8.75%
No relatives	81	6.88%
Total	1177	

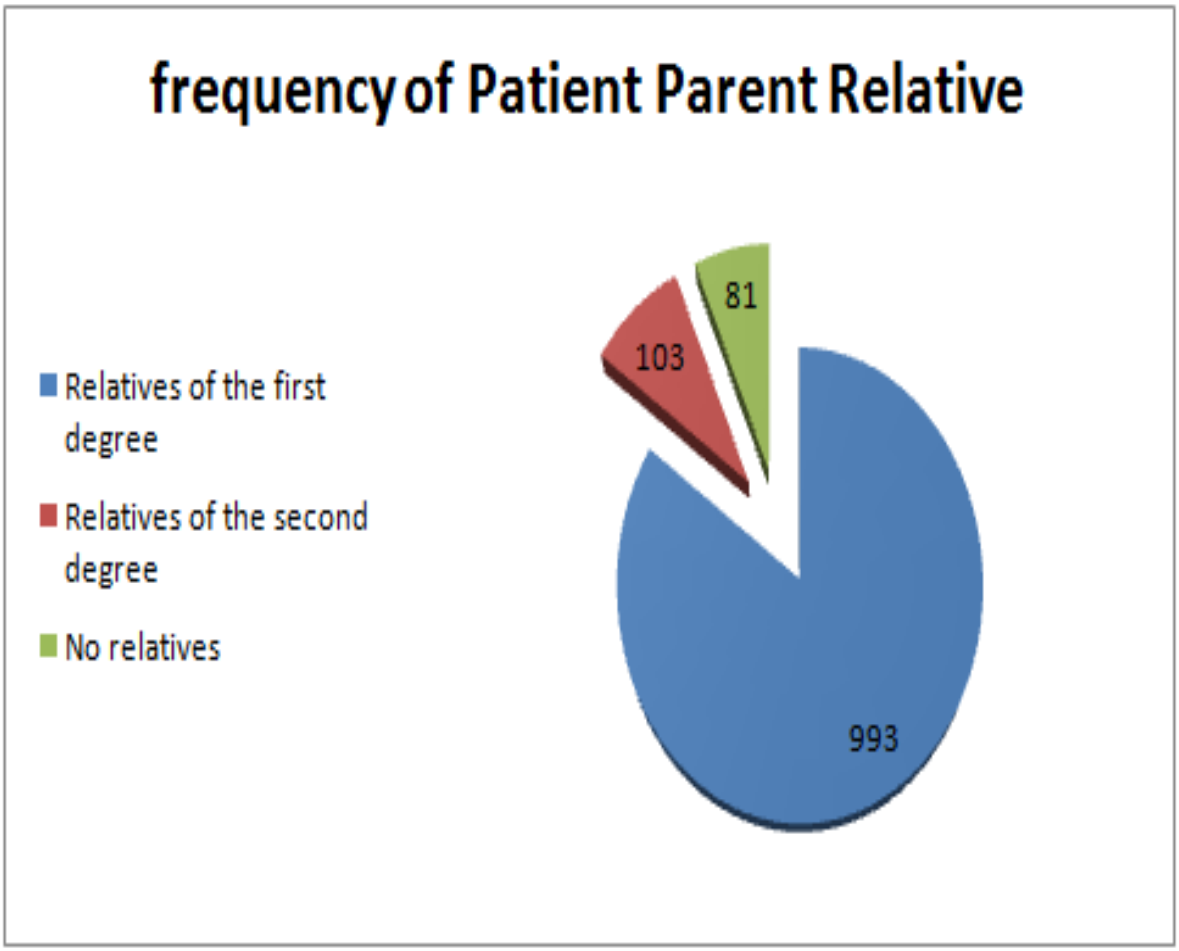


Figure (4.4) pie graph show the frequency of patient parents relative.

Table (4.5): shows the frequency % of Incidence of Prostate Cancer from January 2010 to December 2012 in RICK (SUDAN)

Years	Frequency
2010	**329**
2011	**404**
2012	**444**

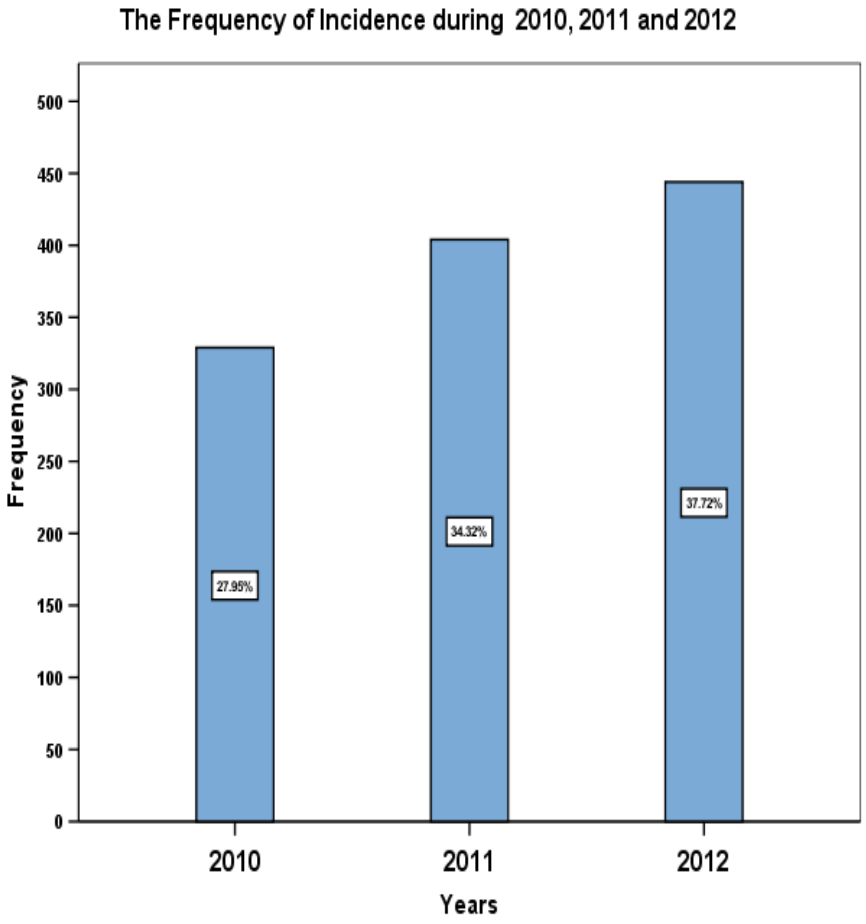


Figure (4.5) Bar graph shows the incidence of prostate cancer during 2010, 2011and 2012

Section two: the correlation between 5 Years Survival Rate with age, grade, type of treatment, site of metastasis and type of cancer cell.

Table (4.6): Observed, corrected and relative cumulative survival rates among Prostate Cancer patients

Years After diagnosis	Observed survival rates	Corrected survival rates	relative survival rates
0	**0.974**	**0.980**	**0.974**
1	**0.735**	**0.751**	**0.835**
2	**0.570**	**0.595**	**0.647**
3	**0.467**	**0.496**	**0.530**
4	**0.389**	**0.420**	**0.442**
≥ 5			

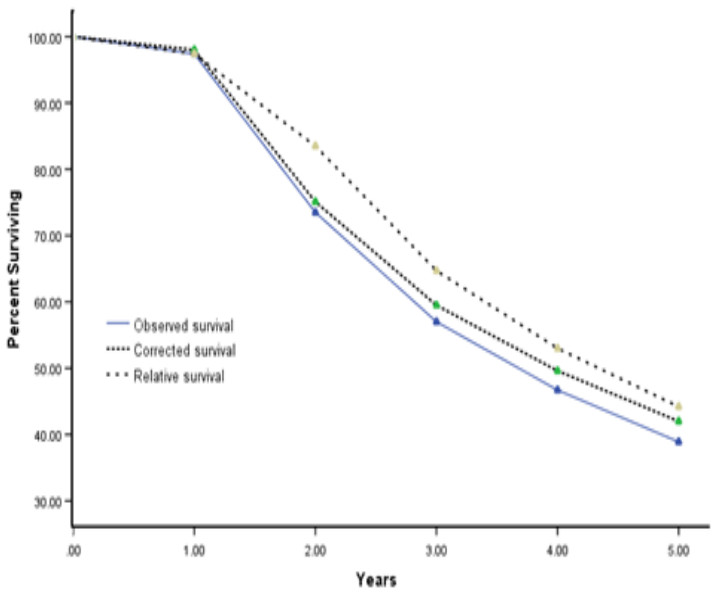


Figure 4.6: Line graph showthe relation between Observed, corrected and relative cumulative survival rates among Prostate Cancer patients

Table (4.7): cross tabulation between treatment and grade

Treatment		Grade				Total
		Will differentiated	Moderately differentiated	Poorly differentiated	Undifferentiated	
	Radiotherapy	0	0	1	1	2
	Hormone therapy	0	0	10	16	26
	Combination S+R	2	2	2	0	6
	Combination S+H	2	3	2	0	7
	Combination R+H	0	2	15	4	22
	Combination S+R+H	10	16	2	1	29
	Combination S+R+H+C	3	5	0	1	8
Total		17	28	32	23	100

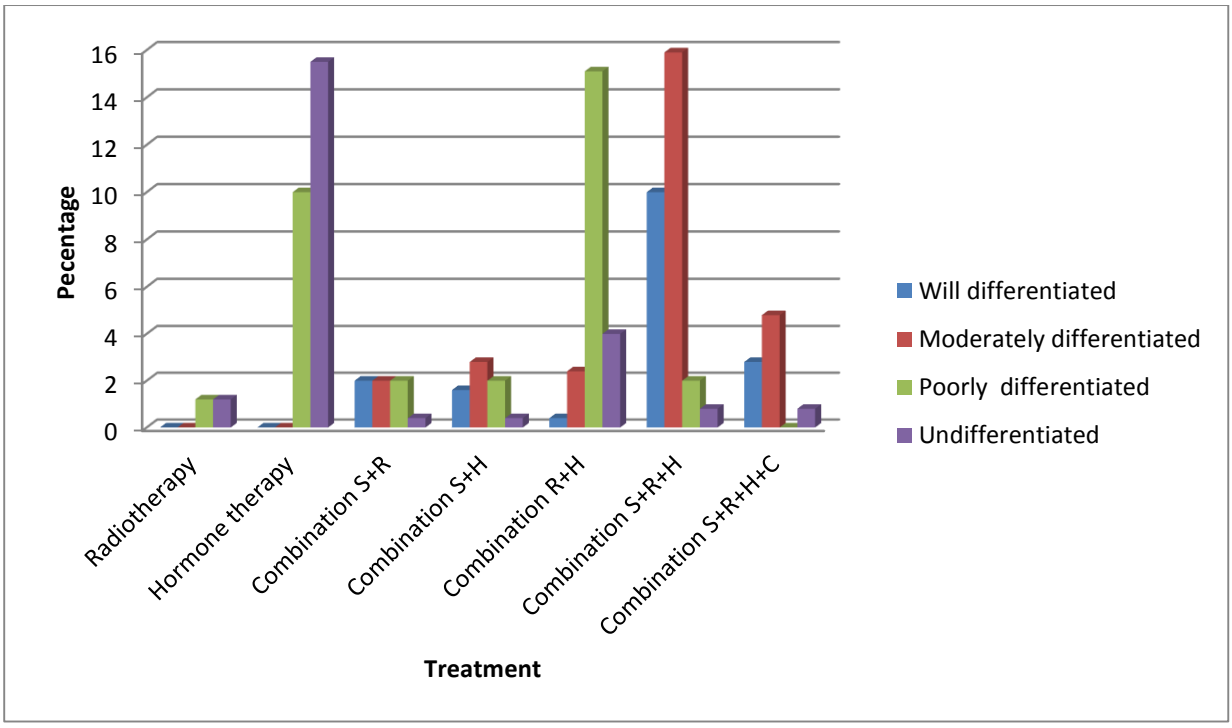


Figure (4.7)bar graph shows the Percentage and relationship between types of treatment with grade.

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Table (4.8): cross tabulation between type of cancer cells and grade

Typeofcancer	Grade				Total
	Will differentiated	Moderately differentiated	Poorly differentiated	Undifferentiated	
Adencarcinoma	17	28	31	15	91
Sq. cell carcinoma	0	0	1	8	9
Total	17	28	32	23	100

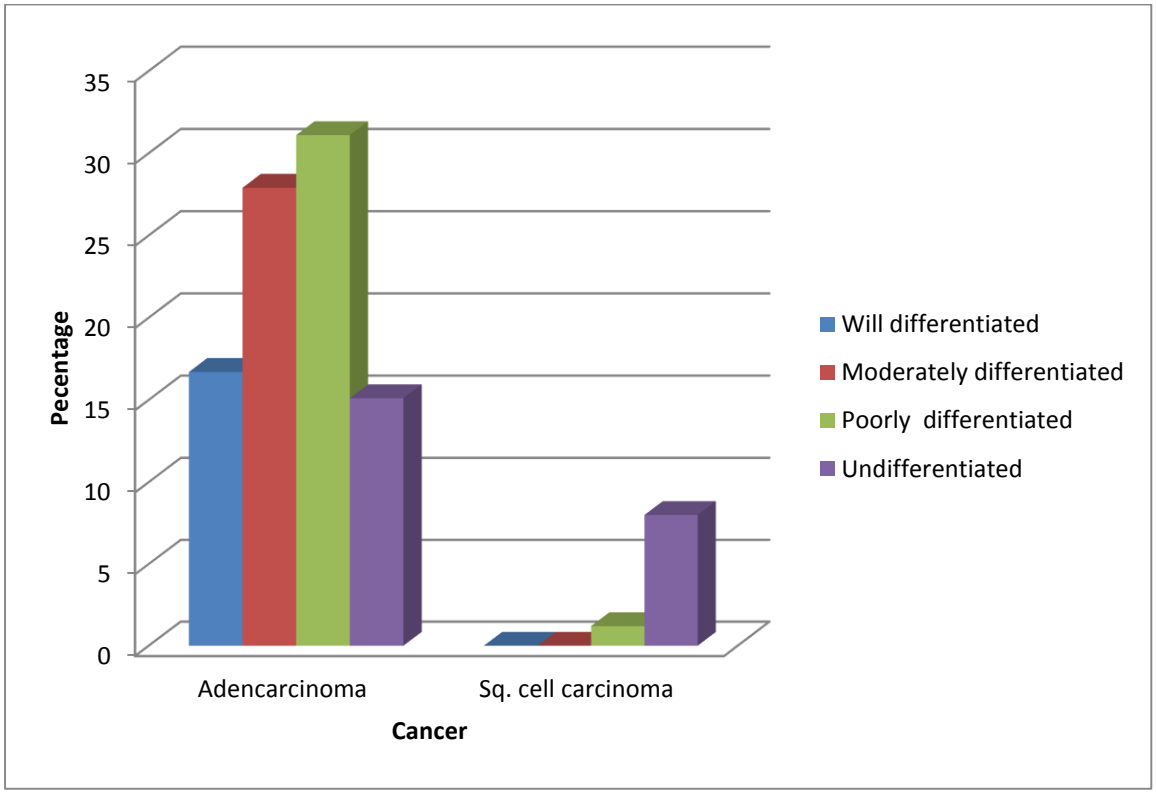

Figure (4.8)bar graph shows the Percentage and relationship between types of cancer cell with grade.

Table (4.9): cross tabulation between site of MITS and grade

Site_of_mits		Grade				
		Will differentiated	Moderately differentiated	Poorly differentiated	Undifferentiated	Total
	No metastasis	16	26	0	0	42
	Spine	0	2	16	6	24
	Pelvic	0	0	11	1	12
	Lymph node	0	0	1	1	2
	Liver	0	0	0	2	2
	more than one site	0	0	4	14	18
Total		17	28	32	23	100

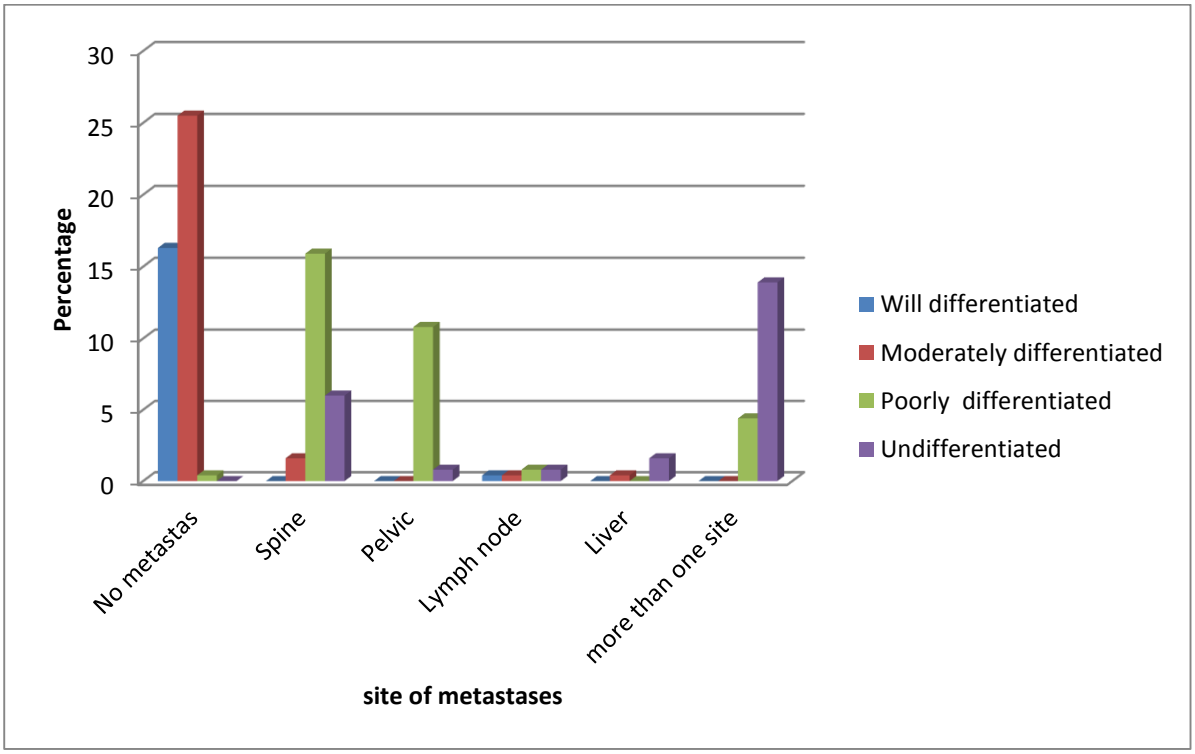

Figure (4.9)bar graph shows the Percentage and relationship between the sites of MITS with grade.

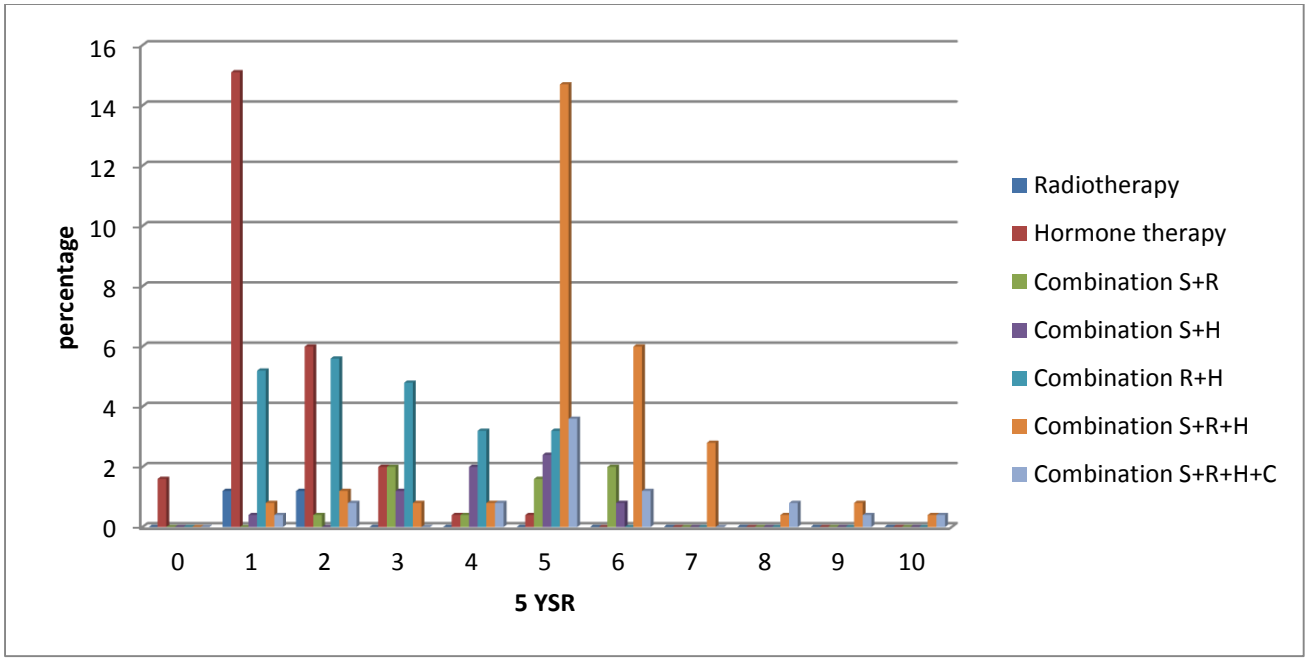

Figure (4.10)bar graph shows the Percentage and relationship between the types of treatment with 5YSR.

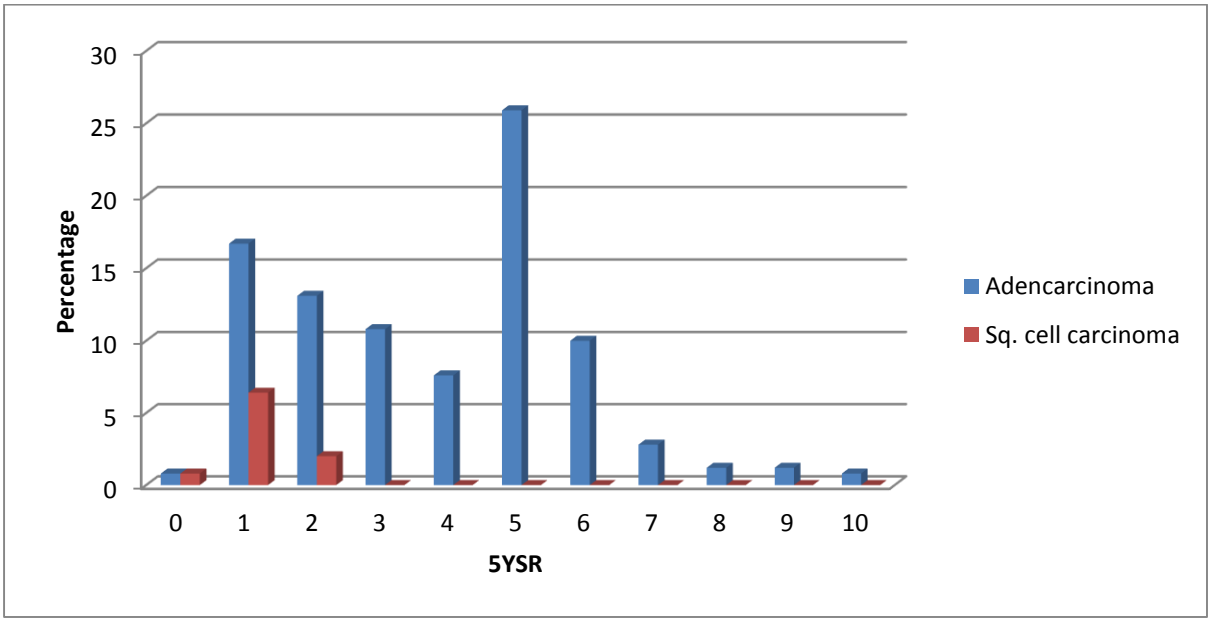

Figure (4.11)bar graph shows the Percentage and relationship between the types of cancer cell with 5YSR.

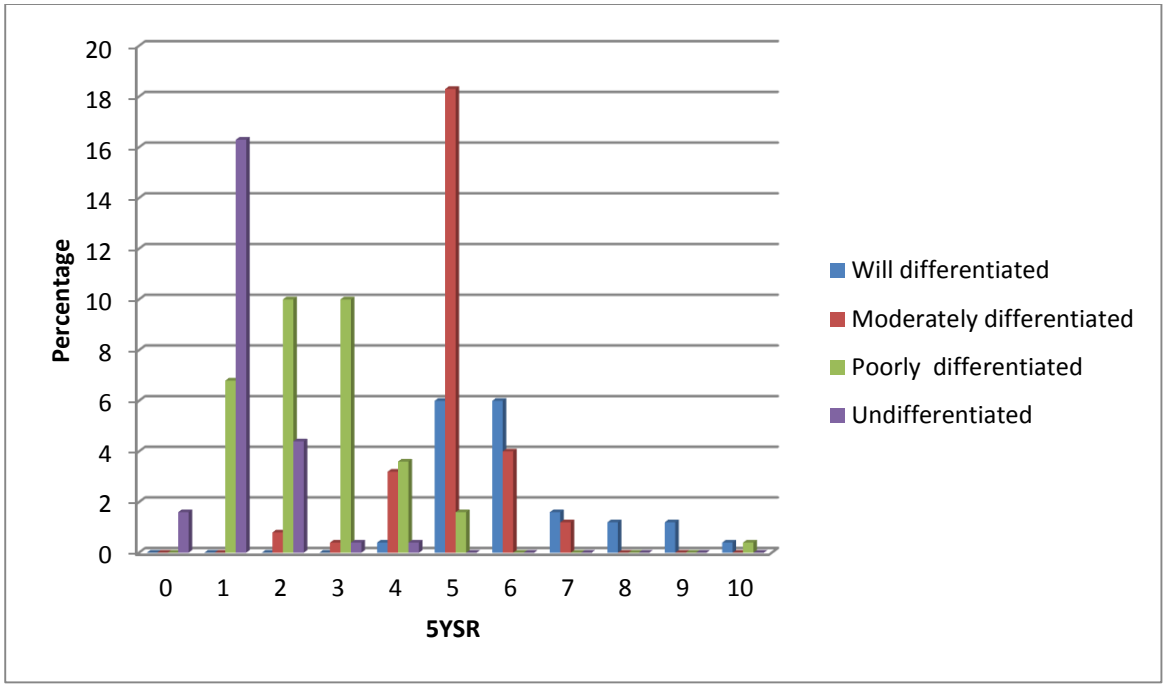

Figure (4.12)bar graph shows the Percentage and relationship between grades with 5YSR.

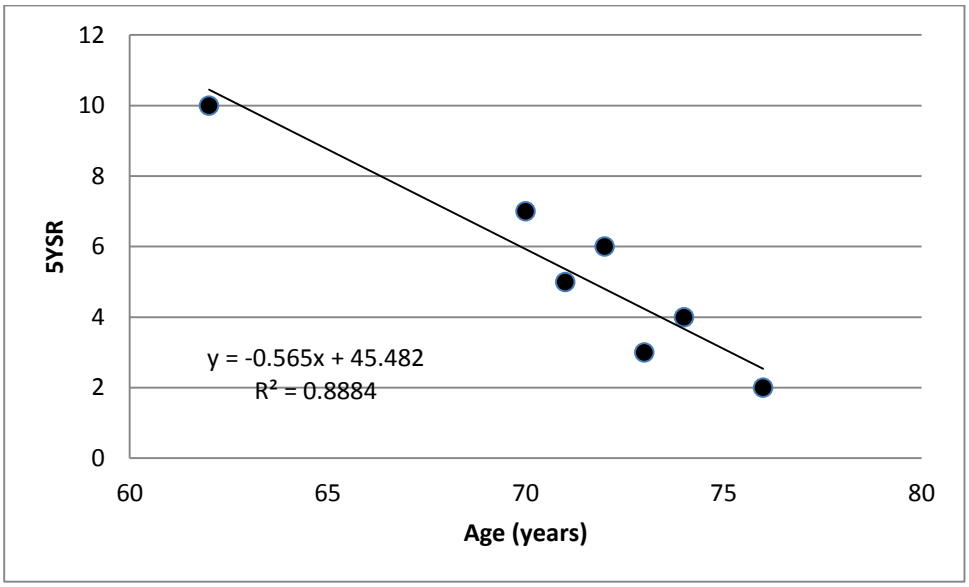

Figure (4.12) line graph shows the correlation between the age and 5YSR.

Chapter five
Discussion, Conclusion and recommendations

5.1 Discussion

Survival rates tell us what percentage of people with the same type and grade of cancer are still alive a certain amount of time (usually 5 years) after they have been diagnosed. This study was a retrospective cohort study, which performed among cancer patients in Sudan. With a sample of 306 patients with prostate cancer. The patients' age ranged between 45-95 years old. The study data was retrieved from patients' files system of Radiation and Isotopes Center of Khartoum (RICK) which included patient age, grade, type of treatment, type of cancer cells and site of tumor MITS. They were followed for years to calculate the 5YSR. There are many methods to measure it, such as direct method, actuarial method and Kalban-Meier method. First measure by the Direct Method (appendix- vital status data sheet),it's the simplest way of summarizing patient survival , by calculate the percentage of patients alive at the end of a specified interval such as five years, using for this purpose only patients exposed to the risk of dying for at least five years.
Examination of the entries in the 'Vital Status' column in (appendix) for the 306 patients at risk for at least five years indicates that 89 Patients were alive at last contact and 217 had died before December 2016. However, one of these patients for example (No.114) had lived five complete years before his death. Therefore, 113 out of 306 patients were alive five years or more after their respective dates of first treatment and, thus, the five-year survival rate is 37%(113 patients).
The direct method for calculating a survival rate does not use all the information available. For example, the data indicate that patient No. 4 died in the fourth year after treatment was started and that patient No. 65 lived for more than four years. That information should be useful, but it could not be used under the rules of the direct method because the patients were diagnosed after June 2011.The actuarial, or life-table, method provides a means for using all the follow-up information

accumulated up to the closing date of the study. The actuarial method has the further advantage of providing information on the survival pattern, that is, the manner in which the patient group was depleted during the total period of observation (Cutler, et al., 1961). The five-year survival rate calculated by the life-table method is 0.389 ≈ 39% (table 3.2).Calculation by Corrected Survival Rate, the observed survival rate calculated for all deaths, not indicates the cause of death, may be some patients died by other reason. Whenever reliable information on cause of death is available, a correction survival rate can be made for deaths due to causes other than the disease under study (Cutler, 1958).Calculation of corrected survival rate (table 3.3), the five-year corrected survival rate is 42%, the corrected rate is particularly important in comparing patient groups, if there are many differences in sample such as age, race and socioeconomic status, which may strongly influence the probability of dying from causes other than the cancer under study, that lead us to measure by other method called relative cumulative survival rates. The Relative survival rate equal Observed survival rate over Expected survival, equal 44 % (table3.4). Also the study found that 661 (56%) of 1177 patients had age group range from 65 to 79 years, Figure (4.1). A rising incidence of microscopic foci of prostate cancer is found in men with increasing age. Results of autopsy studies have shown that almost 30% of men over the age of 50 have histological evidence of prostate cancer (Scardino, 1989). Prostate cancer incidence increases with advancing age; thus, it can be anticipated that the prevalence of prostate cancer in men older than age 65 years will continue to increase. Prostate cancer already is the most common malignancy among older men (A Jemal, 2010) .The common states with a high incidence of prostate cancer were. Khartoum 226 (19%), Kordofan 194(17%), Darfur 157(13.3%) and Northern 148(13%) respectively Figure (4.2), its different from other authors have described the common state which had a high incidence of prostatic disorders was the north state which represents 42%,west state 28% and center state 24% while the east and south were so rare (Mohamed, et al 2013). about 1160(98.5%) of 1177 patients

were a married, table (4.3). and also deals the frequency of patient parents relative found 1096 (93%) of 1177 patients had relation from first and second generation, table (4.4) that indicate to say the prostate cancer may be hereditary , African American men have the highest incidence of prostate cancer in the world (Kathleen, et al, 2004) . In addition the study found from all total patients (1177) that 329(28%) came to treat in Radiation Isotopes Center of Khartoum (RICK) during 2010, 404(34%) and 444(38%) during 2011 and 2012 respectively, Figure (4.5). The detection of new cases of prostate cancer per year at the NCI-UG increased dramatically (from 8.1% of all cancers in 2002 to 17.2% in 2007) after the introduction of transrectal ultrasound (Omran M, et al., 2010). Also in metastasized cancer, bone scans using scintigraphy positively correlated with increased PSA values compared to patients with negative scans ($P < 0.01$) (Khalid, et al., 2011) . Also the study considers the correlation between the grade and the option of treatment, found that patients with Grade I (will differentiated) and Grade II (Moderately differentiated) were commonly treated by protocol surgery combined with radiotherapy and hormone therapy, patient with Grade III (Poorly differentiated) were commonly treated by protocol combination between radiotherapy and hormone therapy and patient with Grade IV (Undifferentiated) commonly treated by option only hormone therapy Figure (4.7). If hormonal therapy is initiated early, the risk of major complications is significantly decreased (Michael, 2006). Also the study concerned in common sites MITS were spine, pelvis and more than one sites are 42%, 24% and 18% respectively. Prostate cancer is known to have high metastatic potential especially to the bone. Bone metastases are common and are osteoblastic in more than 95% (M. A. Long, et al, 1999).

Also the study considers the correlation between the grade and type of cancers cells, found that patients with type of cancer was squamous cell carcinoma commonly associated with grade IV (undifferentiated), also found The common type of prostate cancer cell for is Adencarcinoma 91% and squamous cell

carcinoma 9% Figure (4.8). The study also considers the correlation between kind of treatment protocol, type of cancer cells, grade and age with five years survival rate to determine the affects of these factors for 5YSR.

First of these factors is treatment protocol, commonly when patients treated with protocol combination between (Surgery +Radiotherapy +Hormone therapy) they had a survival rate ≥ five years Figure (4.10). That protocol appears to offer a significant survival advantage over the other treatment options, when selecting the best treatment for patients with clinically localized prostate cancer; one should take into account the general condition of the patient, the natural history of the prostate cancer, the curability of the disease due to type of cancer cells, for example if type of cancer cells were Squamous cell carcinoma the survival rate limited within two years Figure (4.11). Squamous cell carcinoma of the prostate is a rare tumor, making up 0.5% to 1% of all prostate carcinomas. It is typically described as an aggressive cancer (Mott, 1997). Also the study considers the correlation between the grade and age with five years survival rate, found the high-grade prostate cancer greatly reduces Five years survival rate Figure (4.11). and also found when patient increase in age the 5YSR will decrease Figure (4.12). Older patients are more likely to have high-risk prostate cancer at diagnosis and less likely to receive local therapy. Indeed, underuse of potentially curative local therapy among older men with high-risk disease may in part explain observed differences in cancer-specific survival across age strata. These findings support making decisions regarding treatment on the basis of disease risk and life expectancy rather than on chronologic age (Seth K., et al. 2011).

5.2 Conclusion:

The study found that the survival rate of prostate cancer in Sudan were 37%, 42% and 44% ($p > 0.05$) respectively.

The 5YSR for patient with prostate cancer affected with age, grade, and type of treatment option and site of MITS.

Generally the 5YSR for patient with prostate cancer can be estimated according to grade, type of treatment and site of MITS by following Equation:

Survival rate = (-1.396 × Grade)+(0.19 × Treatment)+(-0.105 × Site of MITS)+6.53

Code	Type of treatment
1	Radiotherapy
2	Hormone therapy
3	Combination S+R
4	Combination S+H
5	Combination R+H
6	Combination S+R+H
7	Combination S+R+H+C

Code	Site of metastasis
0	No metastasis
1	Spine
2	Pelvic
3	Lymph node
4	Liver
5	Brain
6	More than one part

Code	Gleason's score sum the primary and secondary	Terminology	Histologic grade
1	2,3,4	Will differentiated	I
2	5,6	Moderately differentiated	II
3	7,8	Poorly differentiated	III
4	9,10	Un differentiated	IV

EX. Patient with prostate cancer (poorly differentiated) with MITS in lumber (L.5) the oncologist decided to treat him by combination (radiotherapy and Hormone therapy) what is expected survival rate ?

Survival rate = (-1.396 × Grade) + (0.19 × Treatment) + (-0.105 × Site of MITS) + 6.53

Survival rate = (-1.396 × 3) + (0.19 × 5) + (-0.105 ×1) + 6.53

Survival rate = (-4.2) + (0.9) + (-0.105) + 6.53

Survival rate = 3.11 years

5.3 Recommendations:

- Can use this equation to measure Survival rate
  Survival rate = (-1.396 × Grade) + (0.19 × Treatment) + (-0.105 × Site of MITS) + 6.53. That can help to improve the survival rate. The sign (-) indicate to decrease the survival rate, while sign (+) indicate to improve the survival rate .
- Screening should be done yearly for men Age 65or more.
- The government must establish centers of screening in all Sudan state to detect the disease in early stage.
- Choose the other treatment options in Sudan to improve the survival rate like cryotherapy because it's better than traditional sugary.
- Review the treatment protocol that use in RICK to treatment the prostate cancer.
- The government must provide the vaccine therapy for prostate cancer.
- Men with a family history of prostate cancer should be done screening at age 45 years.
- Chemotherapy give when hormone therapy not working properly.
- Whole body scan is very necessary to prevent the MITS.
- The hormone therapy alone does not care prostate cancer or don't improve the survival rate.
- Use the Technique of treatment its Preventing and Treating Prostate Cancer Spread to Bones.
- Recommended the researcher to work more research to find out the reasons of prevalence of prostate cancer in Kordofan, Darfur and northern state.

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Appendix I: Data collection sheet

Pt No	Age	Date of Diagnosis month/ year	last contact			complete years lived since diagnosis
			Date (month /year)	vital status	cause of death	
1	60	11/2009	May-16	A	.	7
2	65	7/2009	May-16	D	O	3
3	60	11/2009	May-16	D	C	1
4	80	11/2009	May-16	D	C	4
5	75	1/2010	May-16	D	O	3
6	78	1/2010	May-16	D	C	1
7	75	12/2009	May-16	D	C	1
8	80	12/2009	May-16	D	C	2
9	83	1/2010	May-16	D	O	1
10	60	12/2009	May-16	D	C	1
11	69	1/2010	May-16	D	C	1
12	75	11/2009	May-16	D	C	1
13	90	1/2010	May-16	D	C	4
14	70	1/2010	May-16	D	C	2
15	72	1/2010	May-16	A	.	6
16	57	1/2010	May-16	A	.	6
17	82	12/2009	May-16	A	.	7
18	65	1/2010	May-16	D	C	2
19	72	1/2010	May-16	A	.	6
20	77	1/2010	May-16	D	C	2
21	72	1/2010	May-16	D	C	1
22	78	1/2010	May-16	A	.	6
23	75	12/2009	May-16	D	C	1
24	62	2/2010	May-16	D	C	3
25	64	12/2009	May-16	D	C	3
26	70	1/2010	May-16	D	C	1
27	85	1/2010	May-16	D	C	1

28	70	2/2010	May-16	D	C	1
29	62	2/2010	May-16	D	C	5
30	62	2/2010	May-16	D	C	1
31	75	9/2009	May-16	D	C	1
32	65	10/2009	May-16	D	C	1
33	75	12/2007	May-16	A	.	9
34	71	12/2009	May-16	A	.	7
35	65	1/2010	May-16	D	C	2
36	72	12/2009	May-16	D	C	1
37	57	3/2010	May-16	D	C	1
38	70	1/2010	May-16	A	.	6
39	59	4/2010	May-16	A	.	6
40	75	3/2010	May-16	D	C	6
41	70	1/2010	May-16	D	O	4
42	65	3/2010	May-16	D	C	1
43	65	4/2010	May-16	A	.	6
44	65	6/2010	May-16	D	C	5
45	73	12/2009	May-16	A	.	7
46	80	4/2010	May-16	D	C	2
47	65	2/2010	May-16	D	C	1
48	74	4/2009	May-16	D	C	5
49	69	4/2010	May-16	D	C	3
50	65	12/2009	May-16	D	C	1
51	70	4/2010	May-16	A	.	6
52	76	12/2009	May-16	D	C	3
53	65	5/2010	May-16	D	C	5
54	76	2/2010	May-16	D	C	2
55	75	5/2010	May-16	D	O	1
56	75	6/2010	May-16	D	O	2
57	75	6/2010	May-16	D	C	1
58	70	6/2010	May-16	D	C	2
59	80	6/2010	May-16	D	C	1

60	85	6/2010	May-16	A	.	6
61	80	6/2010	May-16	D	C	4
62	65	8/2009	May-16	A	.	7
63	70	8/2010	May-16	D	C	1
64	65	5/2010	May-16	D	C	1
65	85	5/2010	May-16	A	.	6
66	70	5/2010	May-16	D	C	1
67	82	9/2010	May-16	D	C	6
68	36	8/2010	May-16	D	C	1
69	80	9/2010	May-16	A	.	6
70	82	8/2010	May-16	D	C	6
71	80	9/2010	May-16	D	C	5
72	76	5/2010	May-16	A	.	6
73	70	9/2010	May-16	A	.	6
74	95	4/2010	May-16	D	C	2
75	70	6/2009	May-16	D	C	3
76	65	9/2010	May-16	D	C	3
77	62	9/2010	May-16	D	C	1
78	72	9/2010	May-16	D	C	4
79	70	10/2010	May-16	D	C	2
80	75	8/2009	May-16	D	C	3
81	60	8/2010	May-16	A	.	6
82	80	12/2008	May-16	D	C	2
83	75	10/2010	May-16	D	C	5
84	70	10/2010	May-16	D	C	2
85	78	10/2010	May-16	D	O	1
86	63	3/2008	May-16	A	.	8
87	75	9/2010	May-16	A	.	6
88	59	9/2010	May-16	D	C	1
89	75	9/2010	May-16	D	C	1
90	65	10/2011	May-16	D	C	1
91	77	11/2010	May-16	A	.	6

92	75	11/2010	May-16	D	C	3
93	70	11/2010	May-16	D	C	2
94	65	10/2010	May-16	D	C	1
95	62	10/2010	May-16	D	C	4
96	83	11/2010	May-16	D	C	1
97	70	11/2010	May-16	D	C	5
98	70	12/2010	May-16	A	.	6
99	67	12/2010	May-16	D	C	2
100	77	12/2010	May-16	D	C	1
101	55	10/2010	May-16	D	C	3
102	66	12/2010	May-16	A	.	6
103	63	12/2010	May-16	D	C	2
104	80	12/2010	May-16	D	C	1
105	70	12/2010	May-16	A	.	6
106	66	12/2010	May-16	D	C	1
107	75	1/2011	May-16	D	C	4
108	72	12/2010	May-16	D	C	4
109	74	1/2011	May-16	D	C	4
110	70	1/2011	May-16	D	C	3
111	73	1/2011	May-16	A	.	5
112	89	12/2010	May-16	D	O	3
113	80	9/2010	May-16	D	C	2
114	70	1/2011	May-16	A	.	5
115	65	1/2011	May-16	D	C	1
116	83	1/2011	May-16	D	C	1
117	58	1/2011	May-16	D	C	1
118	71	9/2010	May-16	A	.	6
119	83	1/2011	May-16	D	C	5
120	74	1/2011	May-16	D	C	4
121	65	1/2011	May-16	D	C	1
122	85	1/2011	May-16	D	C	2
123	85	2/2011	May-16	D	C	1

124	58	2/2011	May-16	D	C	4
125	70	12/2011	May-16	D	C	2
126	70	2/2011	May-16	D	C	4
127	74	2/2011	May-16	A	.	5
128	70	2/2011	May-16	A	.	5
129	80	2/2011	May-16	D	C	1
130	78	2/2011	May-16	D	C	5
131	70	2/2011	May-16	A	.	5
132	58	5/2010	May-16	D	C	1
133	93	2/2011	May-16	D	C	1
134	75	8/2010	May-16	D	C	1
135	80	8/2011	May-16	D	C	3
136	85	2/2011	May-16	D	C	3
137	72	2/2011	May-16	D	C	1
138	70	3/1/12	May-16	D	C	3
139	60	2/2011	May-16	D	O	1
140	70	5/2011	Jun-16	D	C	1
141	85	3/2011	Jun-16	D	C	4
142	75	3/2011	Jun-16	D	C	2
143	70	2/2011	Jun-16	D	C	5
144	73	2/2011	Jun-16	D	C	3
145	80	3/2011	Jun-16	D	C	4
146	60	1/2011	Jun-16	D	C	5
147	75	3/2011	Jun-16	D	C	4
148	85	3/2011	Jun-16	D	C	2
149	85	2/2011	Jun-16	D	C	1
150	60	2/2011	Jun-16	D	C	3
151	70	1/2011	Jun-16	D	C	2
152	65	4/2011	Jun-16	D	C	1
153	75	2/2011	Jun-16	A	.	5
154	52	2/2011	Jun-16	D	C	1
155	70	3/2011	Jun-16	A	.	5

156	90	1/2011	Jun-16	D	C	4
157	70	7/12/10	Jun-16	D	C	1
158	82	3/2011	Jun-16	A	.	5
159	75	5/2011	Jun-16	D	C	5
160	70	5/2011	Jun-16	A	.	5
161	65	6/2011	Jun-16	D	C	1
162	86	6/2011	Jun-16	D	C	3
163	85	5/2011	Jun-16	D	C	2
164	70	6/2011	Jun-16	A	.	5
165	72	6/2011	Jun-16	A	.	5
166	56	11/2011	Jun-16	D	O	1
167	85	3/2011	Jun-16	D	C	1
168	71	5/2011	Jun-16	D	C	2
169	65	6/7/11	Jul-16	D	C	1
170	70	6/2011	Jul-16	D	C	1
171	73	7/2011	Jul-16	A	.	5
172	65	6/2011	Jul-16	D	C	3
173	45	5/2011	Jul-16	D	C	1
174	65	4/2011	Jul-16	D	C	1
175	80	6/2011	Jul-16	D	C	1
176	81	7/2011	Jul-16	D	C	4
177	70	8/2011	Jul-16	D	C	1
178	81	7/2011	Jul-16	D	C	2
179	72	6/2011	Jul-16	D	C	1
180	65	7/2011	Jul-16	A	.	5
181	80	7/2011	Jul-16	D	C	4
182	90	7/2011	Jul-16	D	C	2
183	55	3/2011	Jul-16	D	C	1
184	75	8/2011	Jul-16	A	.	5
185	59	8/2011	Jul-16	D	C	1
186	70	8/2011	Jul-16	A	.	5
187	63	6/2011	Jul-16	D	C	2

188	64	11/2010	Jul-16	D	C	3
189	62	7/2009	Jul-16	A	.	7
190	75	8/2011	Jul-16	D	C	3
191	63	9/2011	Jul-16	D	C	2
192	53	9/2011	Jul-16	D	C	2
193	73	9/2011	Jul-16	A	.	5
194	85	7/2011	Jul-16	A	.	5
195	70	9/2011	Jul-16	A	.	5
196	97	9/2011	Jul-16	D	C	1
197	70	10/2011	Jul-16	A	.	5
198	75	10/2011	Jul-16	D	C	3
199	68	10/2011	Jul-16	D	C	0
200	82	10/2011	Jul-16	D	C	1
201	64	9/2011	Sep-16	A	.	5
202	75	9/2011	Sep-16	A	.	5
203	65	11/2011	Sep-16	D	C	2
204	68	11/2011	Sep-16	D	C	4
205	70	11/2011	Sep-16	D	C	2
206	68	6/2011	Sep-16	D	C	2
207	73	10/2011	Sep-16	D	C	1
208	71	11/2011	Sep-16	D	C	1
209	70	5/12/11	Sep-16	A	.	5
210	62	10/2011	Sep-16	D	C	4
211	91	6/12/11	Sep-16	D	C	2
212	73	11/2011	Sep-16	D	C	1
213	77	12/2011	Sep-16	A	.	5
214	70	12/2011	Sep-16	A	.	5
215	80	11/2011	Sep-16	D	C	0
216	75	12/2011	Sep-16	A	.	5
217	85	12/2011	Sep-16	D	C	2
218	75	12/2011	Sep-16	A	.	5
219	65	11/2011	Sep-16	A	.	5

220	80	12/2011	Sep-16	A	.	5
221	62	11/2011	Sep-16	A	.	5
222	86	12/2011	Sep-16	D	C	1
223	65	11/2011	Sep-16	D	C	2
224	70	2/2011	Sep-16	A	.	5
225	60	11/2011	Sep-16	D	C	3
226	85	11/2011	Sep-16	A	.	5
227	76	12/2011	Oct-13	D	O	2
228	75	4/2005	Sep-16	D	C	9
229	70	9/2011	Sep-16	D	C	5
230	68	1/2006	Sep-16	D	C	4
231	65	1/2012	Jan-17	A	.	5
232	90	1/2012	Jan-17	A	.	5
233	60	1/2012	Jan-17	D	O	0
234	70	1/2012	Jan-17	A	.	5
235	70	6/2011	Jan-17	D	C	1
236	86	1/2012	Jan-17	D	C	3
237	65	1/2012	Jan-17	A	.	5
238	58	10/2006	Jan-17	D	C	10
239	85	11/2011	Jan-17	D	C	4
240	55	1/2012	Jan-17	A	.	5
241	65	10/2011	Jan-17	A	.	5
242	62	1/2012	Jan-17	A	.	5
243	80	11/2011	Jan-17	D	C	3
244	75	2/2012	Jan-17	D	C	0
245	77	2/2012	Jan-17	D	C	3
246	65	1/2012	Jan-17	D	C	0
247	62	11/2011	Jan-17	D	C	1
248	72	1/2012	Jan-17	D	C	2
249	48	1/2011	Jan-17	D	C	4
250	75	8/2009	Jan-17	D	O	7
251	57	2/2010	Jan-17	D	C	5

252	72	1/2012	Jan-17	D	C	0
253	70	2/2012	Jan-17	D	C	2
254	65	2/2012	Jan-17	D	C	0
255	65	8/2010	Jan-17	D	C	4
256	90	2/2011	Jan-17	D	C	3
257	60	9/2011	Jan-17	D	C	5
258	70	2/2012	Jan-17	A	.	5
259	70	10/2011	Jan-17	D	C	2
260	75	6/2011	Jan-17	A	.	6
261	82	2/2012	Jan-17	D	C	2
262	70	1/2012	Jan-17	A	.	5
263	65	1/2011	Jan-17	D	C	3
264	65	6/2004	Jan-17	D	C	10
265	80	3/2004	Jan-17	D	O	9
266	75	8/2011	Jan-17	D	C	3
267	60	4/2012	Jan-17	D	C	2
268	65	4/2012	Jan-17	D	C	2
269	90	8/2/10	Jan-17	D	C	2
270	75	3/2012	Jan-17	A	.	5
271	73	3/2012	Jan-17	D	O	0
272	75	4/2012	Jan-17	D	C	2
273	75	7/2011	Jan-17	D	C	4
274	66	4/2012	Feb-17	A	.	5
275	80	4/2012	Feb-17	A	.	5
276	75	4/2012	Feb-17	A	.	5
277	85	9/2011	Feb-17	D	C	1
278	91	4/2012	Feb-17	D	C	2
279	61	9/2011	Feb-17	A	.	5
280	75	4/2012	Feb-17	D	C	1
281	75	4/2012	Feb-17	A	.	5
282	85	4/2012	Feb-17	D	C	2
283	70	11/2011	Feb-17	D	C	3

284	75	5/2012	Feb-17	D	O	2
285	70	4/2008	Feb-17	D	O	8
286	64	5/2012	Feb-17	D	C	2
287	90	5/2012	Feb-17	A	.	5
288	86	5/2012	Feb-17	D	C	3
289	75	2/2012	Feb-17	D	C	1
290	69	5/2012	Feb-17	A	.	5
291	73	5/2012	Feb-17	D	C	2
292	75	2/2011	Feb-17	D	O	4
293	85	10/2006	Feb-17	D	O	8
294	75	5/2012	Feb-17	D	O	2
295	75	5/2012	Feb-17	A	.	5
296	80	8/2010	Feb-17	D	C	5
297	75	10/2011	Feb-17	D	C	2
298	62	6/2011	Feb-17	D	C	5
299	80	6/2012	Feb-17	A	.	5
300	70	6/2012	Feb-17	A	.	5
301	85	4/2012	Feb-17	D	C	2
302	72	6/2012	Feb-17	D	C	3
303	72	6/2012	Feb-17	A	.	5
304	80	6/2008	Feb-17	D	C	6
305	65	6/2011	Feb-17	A	.	6
306	62	6/2012	Feb-17	A	.	5

A: alive, D: dead, C: prostate cancer, O: other.

Appendix II: Data collection sheet 2

PT NO	Age	File no	Treatment			complete years lived since diagnosis	Type of cancer	Grade	Site of metastasis
			S	RT	H				
1									
2									
3									
4									
5									
6									
7									
8									
9									
10									

Code	Type of treatment
1	Radiotherapy
2	Hormone therapy
3	Combination S+R
4	Combination S+H
5	Combination R+H
6	Combination S+R+H
7	Combination S+R+H+C

Code	Site of metastasis
0	**No metastasis**
1	**spine**
2	**Pelvic**
3	**Lymph node**
4	**Liver**
5	**Brain**
6	**More than one part**

Code	The type of cancer
1	**Adenocarcinoma**
2	**Small cell carcinoma**

Code	Gleason's score sum the primary and secondary	Terminology	Histological grade
1	**2,3,4**	**Will differentiated**	**I**
2	**5,6**	**Moderately differentiated**	**II**
3	**7,8**	**Poorly differentiated**	**III**
4	**9,10**	**Un differentiated**	**IV**

Appendix III: some cases of whole bone scan with their report from (RICK)

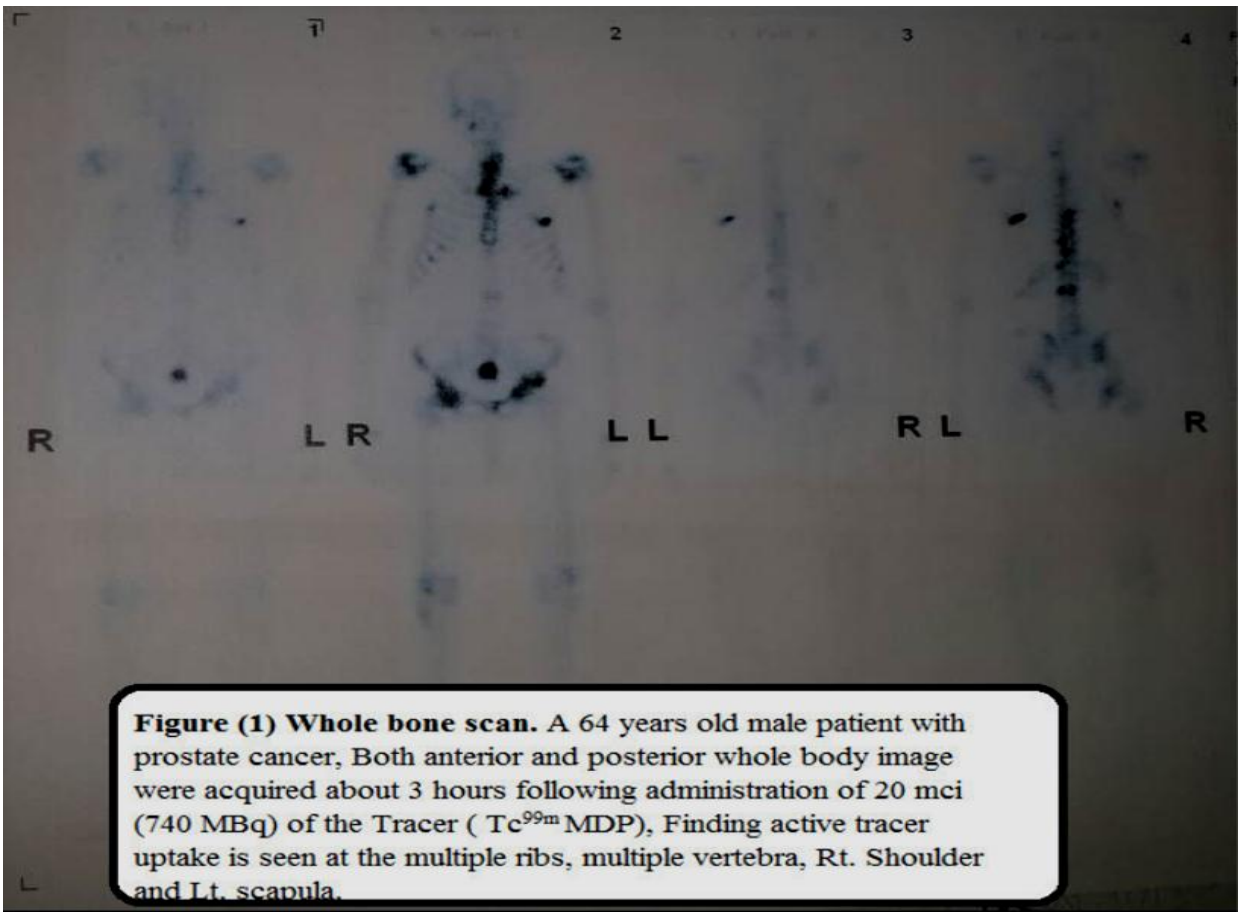

Figure (1) Whole bone scan. A 64 years old male patient with prostate cancer, Both anterior and posterior whole body image were acquired about 3 hours following administration of 20 mci (740 MBq) of the Tracer (Tc^{99m} MDP), Finding active tracer uptake is seen at the multiple ribs, multiple vertebra, Rt. Shoulder and Lt. scapula.

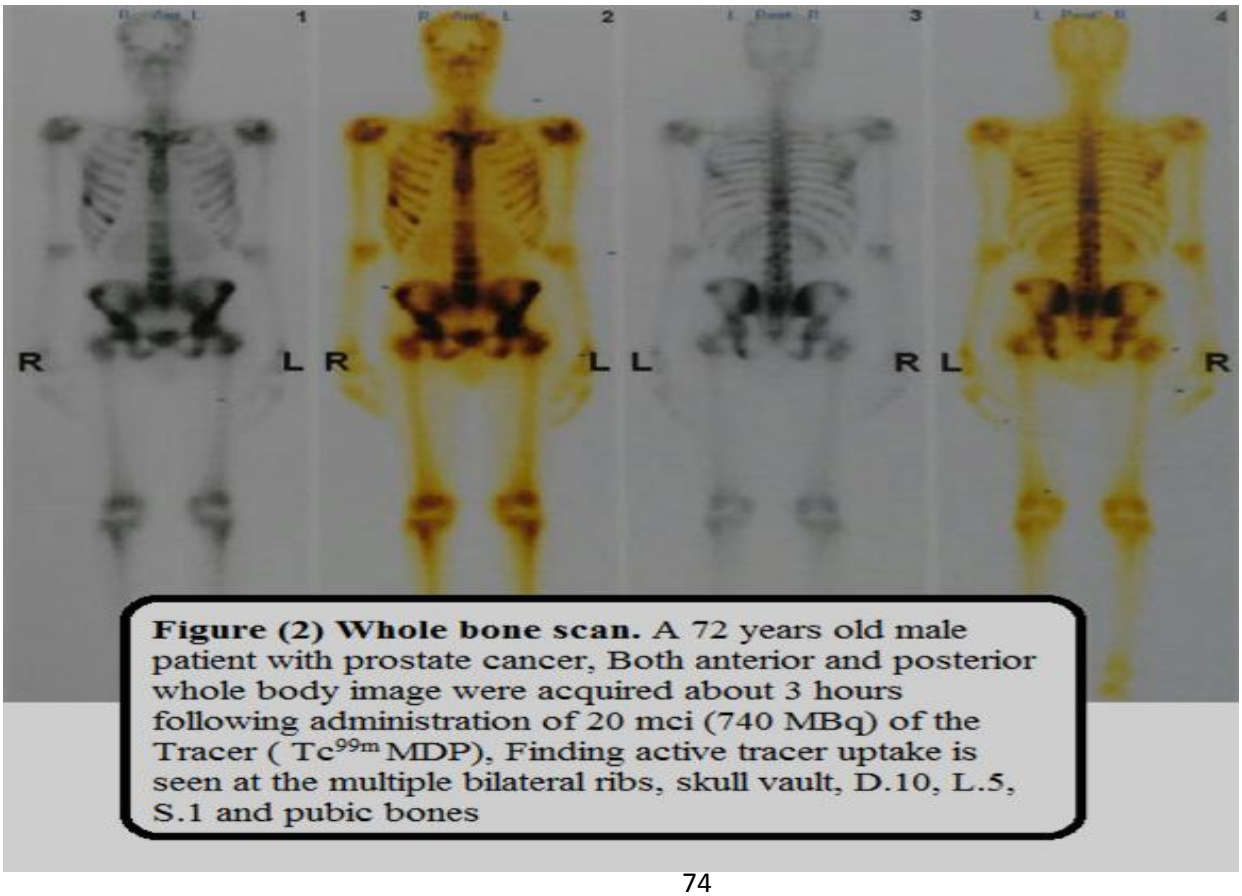

Figure (2) Whole bone scan. A 72 years old male patient with prostate cancer, Both anterior and posterior whole body image were acquired about 3 hours following administration of 20 mci (740 MBq) of the Tracer (Tc^{99m} MDP), Finding active tracer uptake is seen at the multiple bilateral ribs, skull vault, D.10, L.5, S.1 and pubic bones

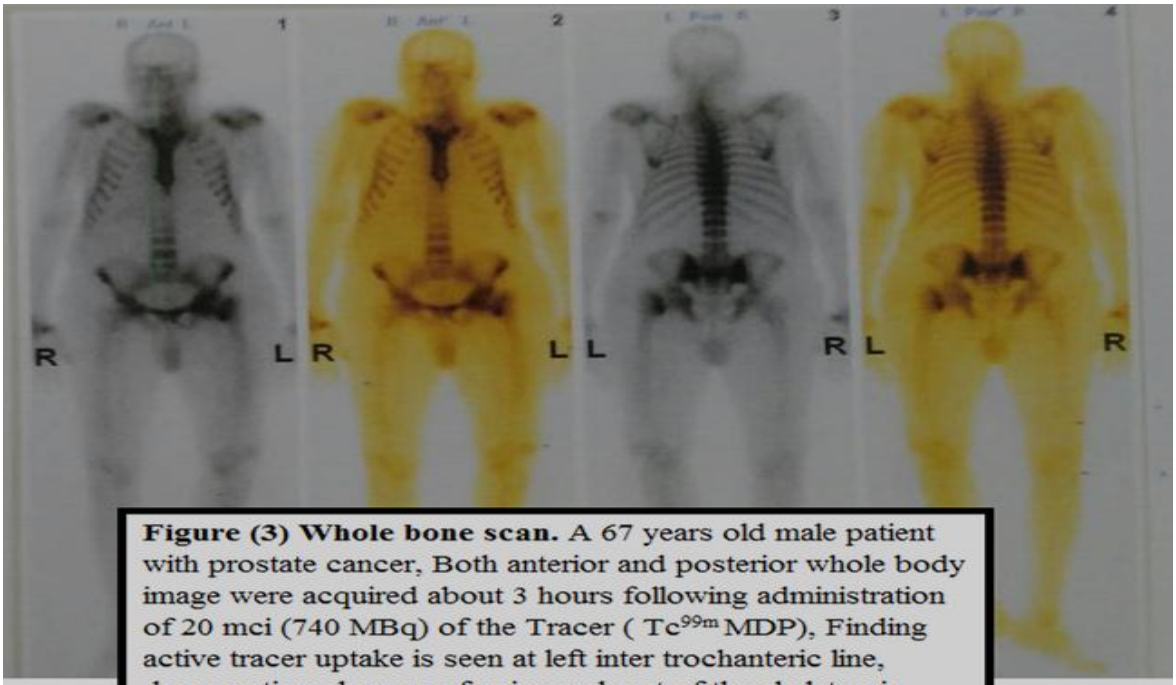

Figure (3) Whole bone scan. A 67 years old male patient with prostate cancer, Both anterior and posterior whole body image were acquired about 3 hours following administration of 20 mci (740 MBq) of the Tracer (Tc^{99m} MDP), Finding active tracer uptake is seen at left inter trochanteric line, degeneration changes of spine and rest of the skeleton is unremarkable

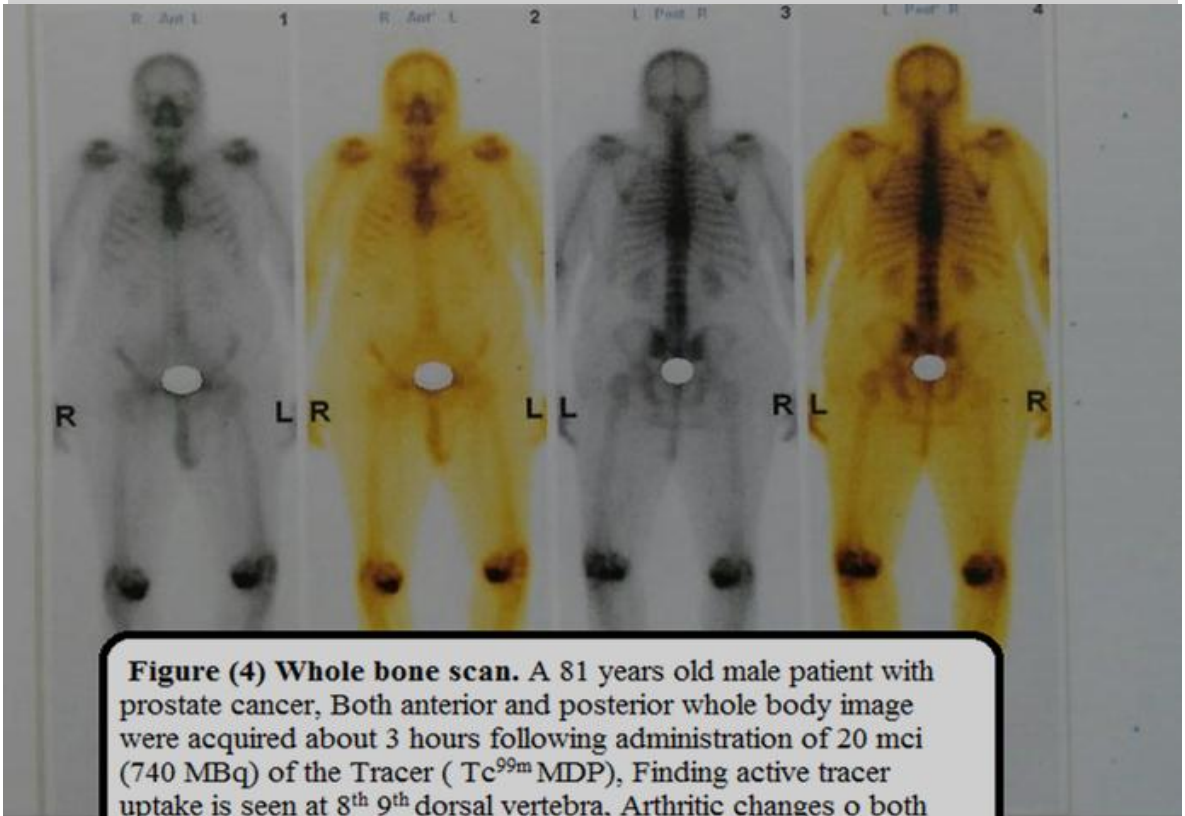

Figure (4) Whole bone scan. A 81 years old male patient with prostate cancer, Both anterior and posterior whole body image were acquired about 3 hours following administration of 20 mci (740 MBq) of the Tracer (Tc^{99m} MDP), Finding active tracer uptake is seen at 8^{th} 9^{th} dorsal vertebra, Arthritic changes o both knees and rest of the skeleton is unremarkable

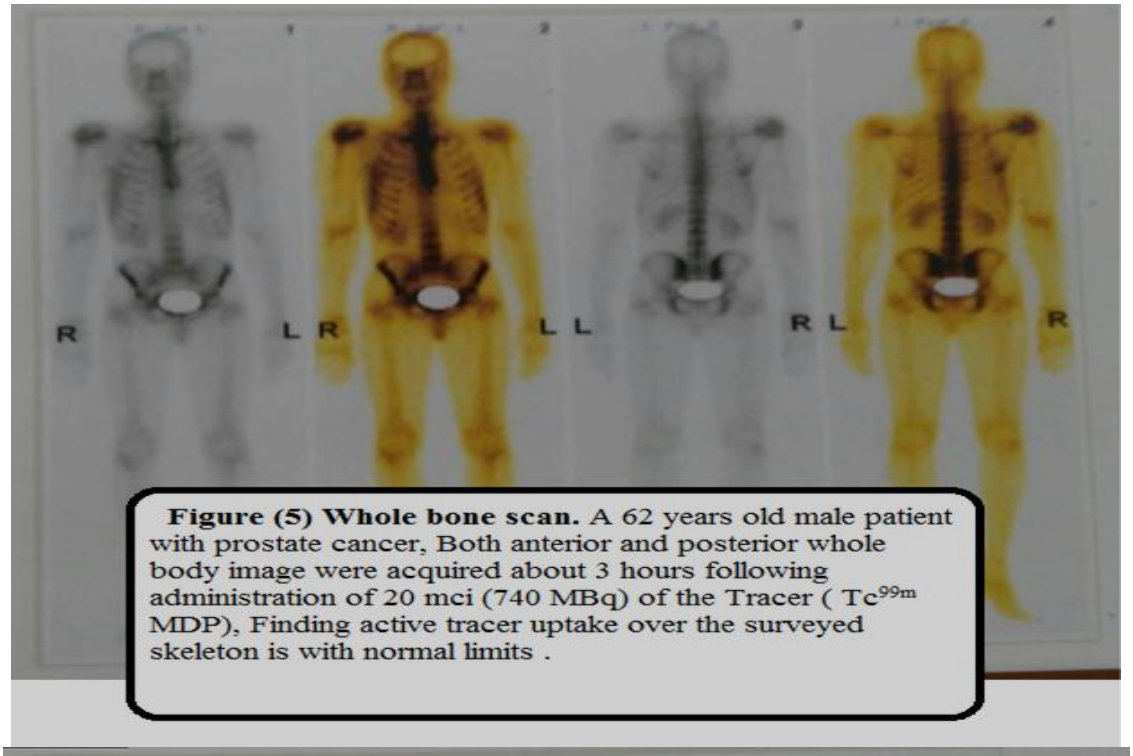

Figure (5) Whole bone scan. A 62 years old male patient with prostate cancer, Both anterior and posterior whole body image were acquired about 3 hours following administration of 20 mci (740 MBq) of the Tracer (Tc^{99m} MDP), Finding active tracer uptake over the surveyed skeleton is with normal limits .

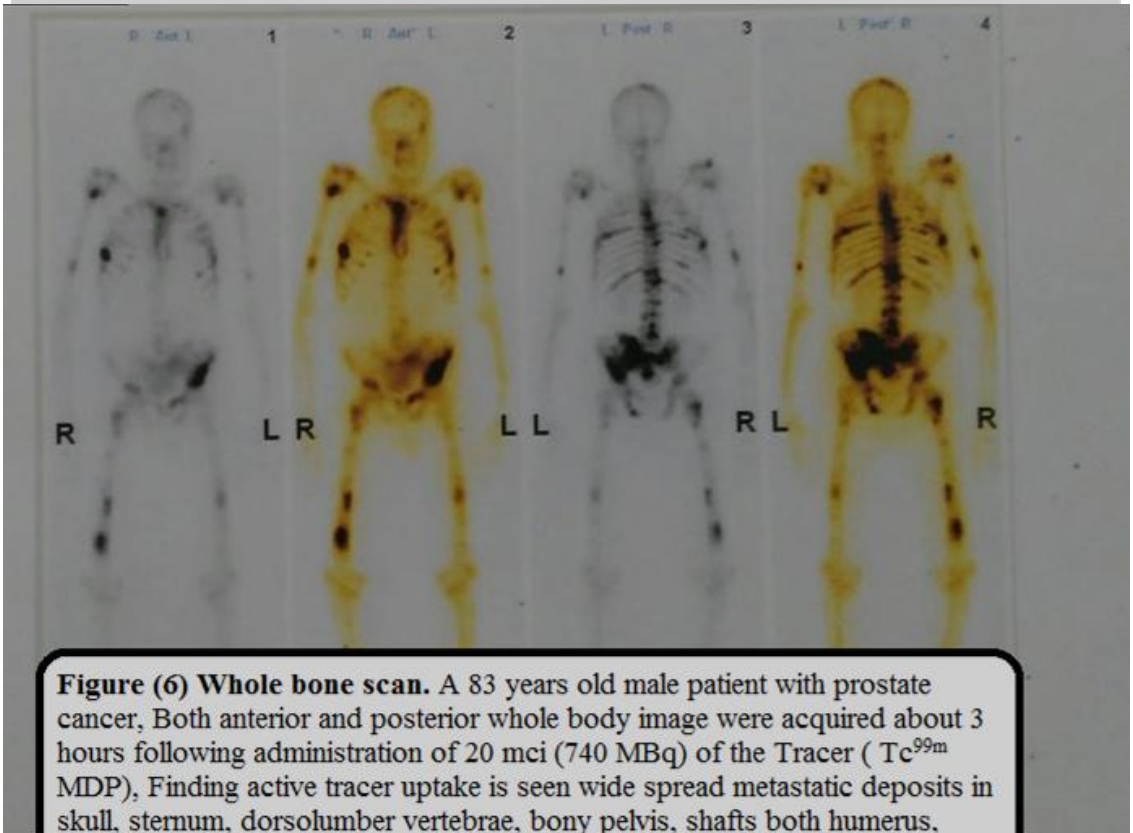

Figure (6) Whole bone scan. A 83 years old male patient with prostate cancer, Both anterior and posterior whole body image were acquired about 3 hours following administration of 20 mci (740 MBq) of the Tracer (Tc^{99m} MDP), Finding active tracer uptake is seen wide spread metastatic deposits in skull, sternum, dorsolumber vertebrae, bony pelvis, shafts both humerus, shoulders, femurs and ribs.

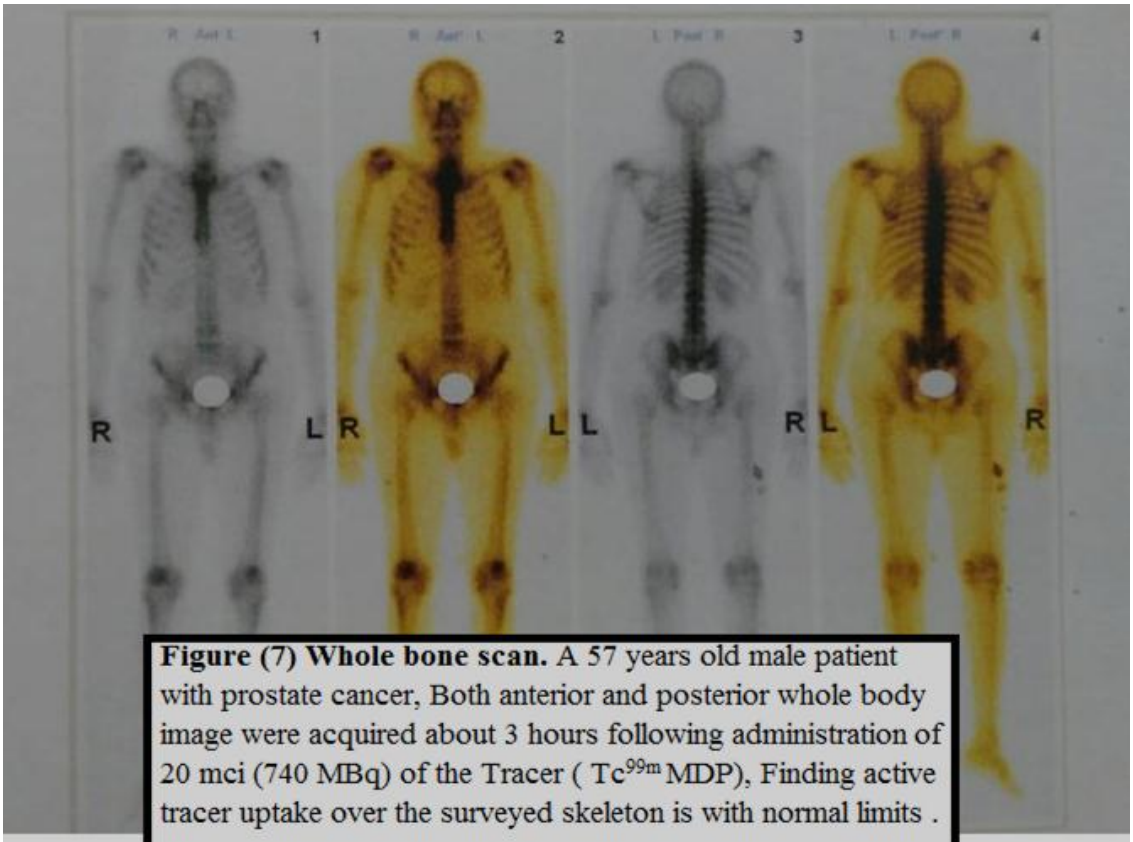

Figure (7) Whole bone scan. A 57 years old male patient with prostate cancer, Both anterior and posterior whole body image were acquired about 3 hours following administration of 20 mci (740 MBq) of the Tracer (Tc^{99m} MDP), Finding active tracer uptake over the surveyed skeleton is with normal limits .

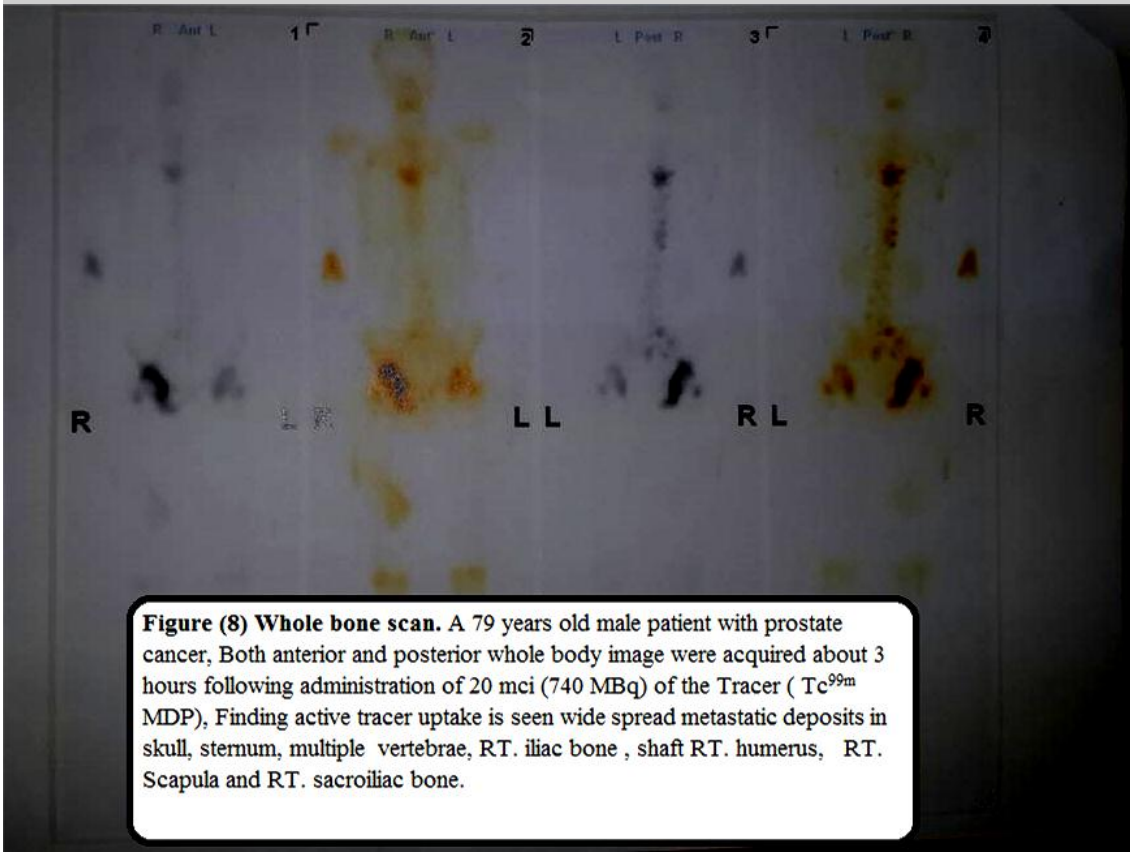

Figure (8) Whole bone scan. A 79 years old male patient with prostate cancer, Both anterior and posterior whole body image were acquired about 3 hours following administration of 20 mci (740 MBq) of the Tracer (Tc^{99m} MDP), Finding active tracer uptake is seen wide spread metastatic deposits in skull, sternum, multiple vertebrae, RT. iliac bone , shaft RT. humerus, RT. Scapula and RT. sacroiliac bone.

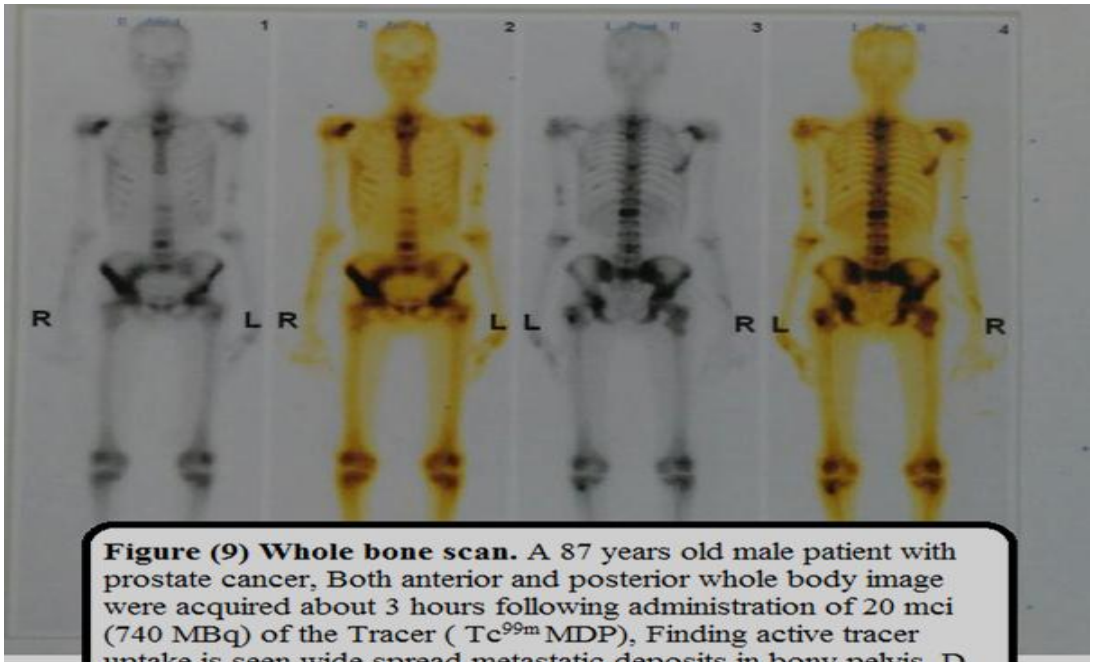

Figure (9) Whole bone scan. A 87 years old male patient with prostate cancer, Both anterior and posterior whole body image were acquired about 3 hours following administration of 20 mci (740 MBq) of the Tracer (Tc^{99m} MDP), Finding active tracer uptake is seen wide spread metastatic deposits in bony pelvis, D. vertebral (1^{st} 3^{rd} 7^{th} 10^{th}), L. vertebral (1^{st} 4^{th}), both femur, multiple , both shoulders , shaft LT. humerus, RT. Scapula and left ribs posteriorly

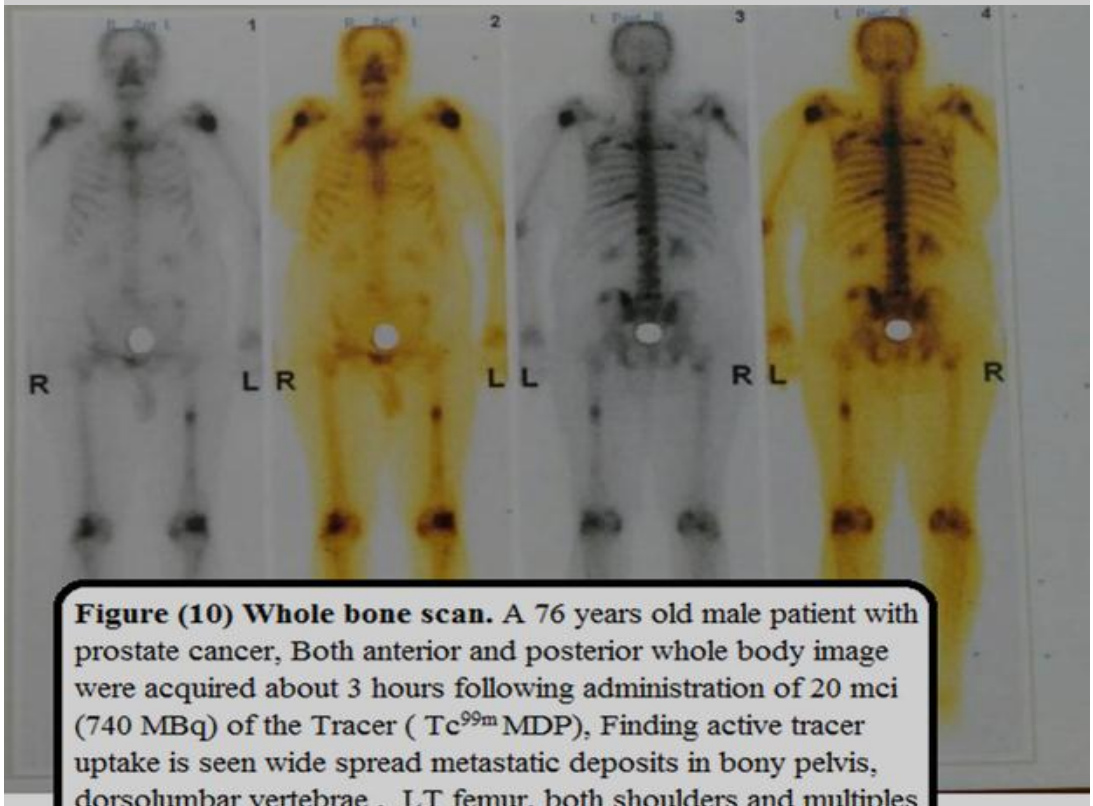

Figure (10) Whole bone scan. A 76 years old male patient with prostate cancer, Both anterior and posterior whole body image were acquired about 3 hours following administration of 20 mci (740 MBq) of the Tracer (Tc^{99m} MDP), Finding active tracer uptake is seen wide spread metastatic deposits in bony pelvis, dorsolumbar vertebrae , LT femur, both shoulders and multiples ribs posteriorly .

Appendix IV: publications